TREATMENT WITH A GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONIST EXENATIDE DECREASES ALBUMINURIA IN OVERWEIGHT TYPE 2 DIABETIC PATIENTS

Tomislav Bulum, Ingrid Prkačin, Lea Duvnjak
Merkur University Hospital, University of Zagreb, School of Medicine, Zagreb, Croatia

INTRODUCTION

Glucagon like peptide-1 (GLP-1) is a gut incretin hormone that stimulates insulin secretion from pancreatic β-cell in a glucose-dependent manner. In kidney, the GLP-1 receptors are expressed in glomerular capillary and vascular walls. Oxidative stress produced by chronic hyperglycemia has a central role in the development and progression of diabetic nehropathy. There is evidence from animal studies that treatment with glucagon-like peptide-1 (GLP-1) receptor agonist exenatide suppressed the progression of diabetic nephropathy with mechanisms that seem to be independent of their glucose-lowering effect. The aim of this study was to investigate effects of exenatide therapy on renal function parameters in overweight type 2 diabetic patients.

SUBJECTS AND METHODS

A total of 43 overweight type 2 diabetic patients with normal, mildly or moderate decreased (estimated GFR ≥ 30 $mlmin^{-1}1.73\ m^2$) renal function were included in this study and followed for 7 months (age 57±7 years, 22M/21F, body mass index (BMI) 36.4±5.1 kg/m^2, weight 114±18 kg, HbA1c 8.6±1.2%, duration of diabetes 11±6 years, serum creatinine 74±23 umol/L, estimated GFR 89±18 $mlmin^{-1}1.73\ m^2$, urinary albumin excretion rate (UAE) 19.5 (2.5-2455.2) mg/24h. UAE was measured from at least two 24-h urine samples. Estimated GFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula. Microalbumin was measured spectrophotometrically by turbidimetric immuno-inhibition. Exenatide was started as 5 mcg twice daily and increased to 10 μg twice daily if needed in patients with estimated GFR ≥ 60 $mlmin^{-1}1.73m^2$.

RESULTS

Treatment with exenatide caused, as expected, a significant decrease in HbA1c from 8.6±1.2 to 8.0±1.3% (p=0.01), BMI from 38±5 to 36±5 kg/m^2 (p<0.001), weight from 114±18 to 106±18 kg (p<0.001), and in waist circumference from 119±12 to 115±11 cm (p<0.001). However, the 22-month administration of exenatide caused a significant decrease in UAE from 19.5 (2.5-2455.2) to 17.2 (3.4-1851.2) mg/24h (p=0.02), while serum creatinine (from 74±23 to 73±23 umol/L (p=0.1)) and estimated GFR (from 89±18 to 90±17 $mlmin^{-1}1.73m^2$ (p=0.2)) did not significantly changed.

Table 1: Differences in clinical study measurements at the study entry and after 7 months in the group of patients treated with exenatide

N=43	Baseline	End of study	p
BMI (kg/m^2)	38±5	36±5	<0.001
Waist circumference (cm)	119±12	115±11	<0.001
Weight (kg)	114±18	106 ±18	<0.001
HbA1c (%)	8.6±1.2	8.0±1.3	0.01

Table 2: Differences in parameters of kidney function at the study entry and after 7 months in the group of patients treated with exenatide

N=43	Baseline	End of study	p
Serum creatinine (umol/L)	74±23	73±23	0.1
eGFR (ml/min)	89±18	90±17	0.2
Albuminuria (mg/24h)	19.5 (2.5-2455.2)	17.2 (3.4-1851.2)	0.02

CONCLUSION

The results of our study suggest that therapy with GLP-1 receptor agonist exenatide may significantly reduce UAE in overweight type 2 diabetic patients. It has been suggested that GLP-1 agonists has a crucial role in protection against increased renal oxidative stress under chronic hyperglycemia via inhibition of NAD(P)H oxidase and protein kinase A activation which resulted in reduced albuminuria and mesangial expansion.

DOI: 10.3252/pso.eu.53era.2016