THE GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONIST LIRAGLUTIDE DECREASE ALBUMINURIA IN OVERWEIGHT TYPE 2 DIABETIC PATIENTS

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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 liraglutide suppressed the progression of diabetic nephropathy with mechanisms that seem to be independent of their glucose-lowering effect. Liraglutide shares a 97% structural homology with human GLP-1 and undergoes a generalized proteolysis without elimination *via* the kidneys. The aim of this study was to investigate effects of liraglutide therapy on renal function parameters in overweight type 2 diabetic patients.

SUBJECTS AND METHODS

A total of 42 overweight type 2 diabetic patients with normal or mildly decreased (estimated GFR ≥ 60 mlmin-11.73 m2) renal function were included in this study and followed for 7 months (age 58 7 years, 18M/24F, body mass index (BMI) 38.5 5.6 kg/m2, weight 111 21 kg, HbA1c 8.1 0.9%, duration of diabetes 13 6 years, serum creatinine 71 15 umol/L, estimated GFR 90 13 mlmin-11.73 m2, urinary albumin excretion rate (UAE) 19.9 (3.2-6250.1) 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. Liraglutide was started as 0.6 mg once daily dose and increased up to 1.8 mg once daily.

RESULTS

Treatment with liraglutide caused, as expected, a significant decrease in BMI from 38 5 to 36 6 kg/m2 (p<0.001), weight from 111 21 to 106 23 kg (p<0.001), and in waist circumference from 120 14 to 114 15 cm (p=0.006), while HbA1c (from 8.1 0.9 to 8.0 1.3% (p=0.01)) did not significantly changed (Table 1). However, the 7-months administration of liraglutide caused a significant decrease in UAE from 19.9 (3.2-6250.1) to 17.3 (7.5-420.1) mg/24h (p=0.04), while serum creatinine (from 71 15 to 76 19 umol/L (p=0.3)) and estimated GFR (from 90 13 to 88 18 mlmin-11.73m2 (p=0.3)) did not significantly changed (Table 2).

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

N=42	Baseline	End of study	p
BMI (kg/m2)	38±9	36±6	<0.001
Waist circumference (cm)	120 (96-158)	110 (96-151)	0.006
Weight (kg)	111±21	106 ±23	<0.001
HbA1c (%)	8.1±0.9	7.5±1.3	0.04

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

N=42	Baseline	End of study	p
Serum creatinine (umol/L)	72±15	76±19	0.03
eGFR (ml/min)	90±13	88±18	0.3
Albuminuria (mg/24h)	19.9 (3.2-6250.1)	17.3 (7.5-420.1)	0.04

CONCLUSION

The results of our study suggest that therapy with GLP-1 receptor agonist liraglutide may significantly reduce UAE in overweight type 2 diabetic patients. It has been suggested that liraglutide 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.

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