THE ANTIPROTEINURIC EFFECT OF SITAGLIPTIN IN PATIENTS WITH DIABETIC NEPHROPATHY

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Objectives:

Proteinuria is an important risk factor for progression of chronic kidney disease (CKD). The reduction in proteinuria is also established to slow the progressive reduction in glomerular filtration rate (GFR). Although angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) are known to decrease proteinuria (1,2), most patients progress to end stage renal disease. Sitagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, has some favourable effects beyond its glucose lowering effect. However, little is known about the effect of sitagliptin on urinary protein excretion. The aim of the study was to investigate antiproteinuric effect of sitagliptin in patients with diabetes nephropathy.

Methods:

This study was performed in 50 (29 female and 21 male) patients with diabetic nephropathy. Body mass index (BMI), systolic and diastolic blood pressure (BP) and biochemical tests including fasting and postprandial blood glucose (FBG and PBG respectively), hemoglobin A1c (HbA1c), high-sensitivity C-reactive protein (hsCRP), lipid profile, 24-h urinary protein excretion were obtained at the beginning and at the end of the study. GFR was calculated according to the abbreviated modification of diet in renal disease (MDRD) formula. Patients received sitagliptin (100 mg/d) for 12 weeks. All the analysis were conducted using SPSS, Windows version 15.0. $P < 0.05$ was considered to be significant.

Tablo 1. The clinical and laboratory results of the patients before and after treatment

Parameter	Pretreatment	Posttreatment	P
Body mass index (kg/m²)	33.61±6.43	33.62±6.47	0.858
Systolic blood pressure (mmHg)	142.10±18.01	138.70±16.65	0.005
Diastolic blood pressure (mmHg)	85.80±8.65	82.60±7.16	0.001
Fasting plasma glucose (mg/dl)	140.74±27.61	124.00±23.49	<0.001
Postprandial glucose (mg/dl)	194.50 (160-290)	164.50 (69-280)	<0.001
HbA1c (%)	7.11±1.00	6.32±0.85	<0.001
Creatinine clearance (ml/min/1.73m²)	85.76±20.75	85.50±21.80	0.283
Proteinuria (mg/day)	455.50 (243-5980)	300.50 (74-4544)	<0.001
Urea (mg/dl)	33.06±11.18	34.00±8.85	0.439
Creatinine (mg/dl)	0.80±0.16	0.81±0.18	0.468
Uric acid (mg/dl)	5.62±1.36	5.68±1.43	0.885
Albumin (gr/dl)	4.31±0.30	4.28±0.36	0.479
Total cholesterol (mg/dl)	185.65±40.06	179.40±38.20	0.138
Triglycerides (mg/dl)	176.61±95.88	170.18±91.39	0.465
LDL-cholesterol (mg/dl)	105.30±35.63	103.94±33.30	0.481
HDL-cholesterol (mg/dl)	43.20±10.54	43.33±10.83	0.601
Hs-CRP (mg/dl)	0.35 (0.04-5.59)	0.25 (0.04-1.80)	<0.001
Hemoglobin (gr/dl)	13.27±1.57	13.54±1.54	0.107

Results:

Fifthy-five patients were included at the beginning of the study. Three patients due to mild hypoglycaemia, one patient due to malaise and one patient due to headache discontinued sitagliptin. Upper respiratory tract infection was developed in one patient recovering with antibiotic treatment. Pre- and posttreatment data of the patients are summarized in table 1. There were significant reductions in FBG, PBG, HbA1c, hs-CRP, proteinuria, systolic and diastolic BP. However, no correlation was detected between the reduction in proteinuria and reductions in other variables including FBG, PBG, HbA1c, hs-CRP, systolic and diastolic BP. (P=0.087; P=0.482; P=0.094; P=0.463; P=0.430; P=0.892, respectively).

Conclusions:

We found that sitagliptin significantly reduces urinary protein excretion. Furthermore, it exerts antihypertensive and anti-inflammatory properties in addition to its antidiabetic effect. In our patients, the drug was generally well tolerated. DPP-4 inhibitors may decrease BP by increasing glucagon like peptide (GLP-1). GLP-1 increased urinary sodium excretion in obese men with insulin resistance (3). Also, GLP-1(9-36) had a vasodilator effects (4). Sitagliptin demostrated hypotensive effects in diabetic rats (5). It reduced both systolic and diastolic BP in type 2 diabetic patients (6). Sitagliptin has anti-inflammatory properties. Asahara et al have reported sitagliptin both supresssed serum amyloid A-LDL, C-reactive protein, interleukin-6 and tumor necrosis factor-α and increased interleukin-10 (7). Our study showed that sitagliptin significantly decreases proteinuria, which is not associated with reductions in glycemic indices, BP, and inflammatory parameters. Thus, it is possible that there are other mechanisms which decrease protein excretion. Although our important results, further studies are warranted to evaluate the effect of sitagliptin on proteinuria.

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