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Brief report

Atorvastatin ameliorates podocyte injury in patients with type 2 diabetes complicated with dyslipidemia

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ABSTRACT

We examined the effects of atorvastatin on urinary podocyte excretion. Thirteen patients with type 2 diabetes receiving 2.5 mg of rosuvastatin were recruited and the medication was switched to 10 mg of atorvastatin for a 24-week period. With the switch to atorvastatin, the urinary excretion of podocytes was significantly reduced.

1. Introduction

A number of clinical studies have indicated that the 3-hydroxyl-3-methylglutaryl-CoA (HMG-CoA) reductase inhibitor (statin) has favorable effects on renal function by controlling dyslipidemia [1–3]. Furthermore, it has been reported that various statins have a different impact on renal function, especially on diabetic nephropathy (DN) [4].

The detachment of podocytes from the glomerular basement membrane and podocyte loss in the urine are associated with glomerulosclerosis progression [5]. Therefore, monitoring urinary podocytes could be clinically useful [6].

With this in mind, we examined the effect of atorvastatin, a lipophilic statin, on urinary podocytes when rosuvastatin, a hydrophilic statin was switched for atorvastatin.

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2. Methods and research design

2.1. Subjects

Thirteen patients with type 2 diabetes (10 men and 3 women) were recruited in this study (Table 1). All patients had received 2.5 mg rosuvastatin for at least 3 months. We only recruited patients with normo- to microalbminuria and excluded those with macroalbuminuria, hematuria, and collagen diseases. We also recruited patients who were positive for the excretion of urinary podocytes.

2.2. Study design

Statin therapy of diabetic patients positive for the excretion of urinary podocytes was switched from 2.5 mg of rosuvastatin to 10 mg of atorvastatin for a 24-week period, and the effects on urinary podocyte excretion evaluated before and after switching the statin. The present study was conducted in accordance with the ethical principles of the Declaration of Helsinki and was approved by the ethical committee of the School of Medicine, Chiba University prior to its inception. All patients understood the study aims and methods and provided written, informed consent.

2.3. Clinical parameters of blood and urine

Venous blood samples and urine samples were collected at baseline and at the end of the intervention in the morning after a 12-h fast. Fresh samples of first-voided morning urine were collected and urinary podocytes were measured using the U-podocyte test (at Mitsubishi Chemical Medicine) as described previously [7].

Table 1 – Basic characteristics of patients.

Number (men/women)	13 (10/3)
Age (years)	61.3 ± 11.9
Systolic blood pressure (mmHg)	122.4 ± 16.9
Diastolic blood pressure (mmHg)	71.2 ± 1.0
Fasting blood glucose (mg/dl)	158.1 ± 64.4
HbA1c (mmol/mol)	53.7 ± 11.2
HbA1c (%)	7.06 ± 1.04
Serum creatinine (mg/dl)	0.82 ± 0.18
Estimated GFR (ml/min/1.73 m^2)	70.1 ± 19.2
Urinary albumin (μg/g Cre)	28.6 ± 21.4
Uric acid (mg/dl)	5.4 ± 1.6
LDL-C (mg/dl)	97.5 ± 21.9
HDL-C (mg/dl)	51.5 ± 12.1
TG (mg/dl)	169.2 ± 73.4
ARBs (%)	46.2
Sulfonylurea (%)	38.5
αGI (%)	46.1
Metformin (%)	61.5
Thiazolidine (%)	38.5
DPPIV-I (%)	38.6
Insulin (%)	30.7

LDL-C: low density lipoprotein cholesterol, HDL-C: high density lipoprotein cholesterol, ARB: angiotensin II type 1 receptor blocker, αGI: alpha glucosidase inhibitor, DPPIV-I: dipeptidyl peptidase IV inhibitor.

2.4. Statistical analysis

Values are indicated as mean ± standard deviation (SD). A paired *t*-test was used and statistical analyses were performed using SPSS 15.0J (SPSS Japan Inc., Tokyo, Japan). A p-value < 0.05 was considered statistically significant.

3. Results

3.1. Atorvastatin significantly reduces urinary podocyte excretion

As shown in Fig. 1, urinary podocytes were undetected in 10/13 (77%) of patients after a 24-week period of atorvastatin administration. During the study period, there was no change in treatment for diabetes mellitus or hypertension, and there was no difference in lipid levels, glucose metabolism, or blood pressures before or after the statin switch (Table 2). The mean values of the oxidative stress marker, urinary F(2)-isoprostane, tended to decrease without reaching significance. Also, there were no adverse effects and no significant differences in urinary albumin excretion (Table 2) and estimated glomerular filtration rate (eGFR) (Fig. 1) before and after the statin switch.

4. Discussion

In this study in people with type 2 diabetes and urinary podocyte excretion, switching from rosuvastatin to atorvastatin significantly reduced urinary podocyte loss.

A recent meta-analysis has shown that statin therapies can reduce proteinuria and benefit kidney function [1] however the effect varies between statins. For instance, high-dose atorvastatin significantly reduced proteinuria but did not affect renal function, whereas rosuvastatin was associated with a significant decline in renal function and had no effect on proteinuria in patients with type 2 diabetes and moderate

Table 2 – Clinical parameters of patients before and after switching medication to atorvastatin from rosuvastatin.

	Before	After 6 months	p-Value
Urinary podocytes (cells/ml)	0.3 ± 0.2	0.07 ± 0.16	0.002
Estimated GFR (ml/min/1.73 m^2)	70.1 ± 19.2	69.5 ± 20.2	0.94
Urinary albumin (μg/g Cre)	28.6 ± 21.4	30 ± 29.2	0.89
LDL-C (mg/dl)	97.5 ± 21.9	95.4 ± 29.0	0.84
HDL-C (mg/dl)	51.2 ± 10.2	51.5 ± 12.1	0.94
Triglyceride (mg/dl)	169.2 ± 73.4	153.2 ± 55.1	0.53
F(2)-isoprostane (pg/ml)	449.1 ± 175.8	408.5 ± 117.8	0.53
FBS (mg/dl)	158.1 ± 64.5	136.6 ± 44.3	0.33
HbA1c (mmol/mol)	53.7 ± 11.2	51.0 ± 7.7	0.24
HbA1c (%)	7.06 ± 1.04	6.4 ± 0.71	0.5
Systolic blood pressure (mmHg)	122.4 ± 16.9	126.2 ± 18.4	0.59
Diastolic blood pressure (mmHg)	71.2 ± 14.0	70.0 ± 13.5	0.83