

Clinical Research**Effects of telmisartan on hypertensive patients with dyslipidemia and insulin resistance****Dongxiu Xu, Junfa Liu, Cuiling Ji, Liping Zhou, Hong Guo***Department of Cardiology, the First Hospital of Harbin Medical University, Harbin 150001, China.*

Objective To investigate the effects of telmisartan on the blood glucose, blood lipid, blood insulin, and insulin resistance in the hypertensive patients with dyslipidemia, and also its effect on controlling blood pressure. **Patients and Methods** A total of 96 hypertensive patients (34 females, 62 males) with dyslipidemia were included (mean age 51.2 ± 9.6 , range 42-65 years). Patients were randomized to receive either telmisartan 80 mg/day ($n=46$) or enalapril 10 mg/day ($n=50$) for 6 months. The levels of blood pressure (BP), heart rate (HR), and biochemical data were measured before therapy and at the end of the 3-month treatment and 6-month treatment, respectively. Meanwhile, insulin resistance was evaluated by using a homeostasis model assessment of insulin resistance (HOMA-IR) and insulin sensitivity (HOMA-IS). **Results** In the telmisartan group, the mean blood pressure was obviously lower than that of pre-therapy ($P < 0.05$), and the levels of triglyceride (TG), HOMA-IR, and HOMA-IS were all obviously lower than those of pre-therapy and of the enalapril group at the end of the 3-month-treatment period ($P < 0.05$). After 6 months of treatment, the levels of TG, HOMA-IR, and HOMA-IS in the telmisartan group were significantly lower in comparison with those of pre-therapy, the enalapril group ($P < 0.01$), and 3-month-treatment ($P < 0.05$). Post-prandial 12 hour blood glucose (P2HBG) in the telmisartan group decreased significantly after 6-month treatment compared with that of pre-therapy and the enalapril group ($P < 0.05$). The level of high density lipoprotein (HDL) cholesterol was significantly higher after 6-month treatment in the telmisartan group than with pre-therapy and the enalapril group ($P < 0.05$). **Conclusions** Telmisartan could not only control blood pressure steadily and effectively, but also decrease blood TG, increase HDL cholesterol and insulin sensitivity, and lower insulin resistance. (*J Geriatr Cardiol* 2007;4:149-152.)

Key Words telmisartan; hypertension; lipid metabolism; insulin resistance

Introduction

Patients with hypertension are often found to have abnormal blood lipid and blood glucose,¹ so it is ideal to have a medication which can control blood pressure while lowering the lipid and even the blood glucose. The purpose of this study is to observe the effects of the angiotensin II receptor antagonist telmisartan on blood glucose, blood lipid, blood insulin, and insulin resistance in the hypertensive patients, as well as its effect on controlling blood pressure.

Methods**Patients**

We studied 96 hypertensive out-patients (34 females, 62 males) with abnormal blood lipids from January, 2006 to December, 2006 (mean age 51.2 ± 9.6 , range 42-65 years old; duration of hypertension from 2 to 12 years). The diagnosis criteria for these patients were used according to the World Health Organization (WHO) standard, and excluded secondary hypertension, renal insufficiency, diabetes mellitus,

and acute coronary syndrome. The blood pressure of these patients ranged from 145/95 mmHg to 165/105 mmHg.

The study protocol was approved by the hospital ethics committee. All patients gave written informed consent prior to their participation in the study.

Data collection and study design

Sitting blood pressure was measured in the right upper brachial artery for three times with an appropriate mercury sphygmomanometer, after at least 10 minutes of rest.

The patients were randomly divided into two groups: the telmisartan (80mg/day, Boehringer Ingelheim) group (46 patients) and the enalapril (10mg/day, MSD, China) group (50 patients). The levels of blood pressure (BP), heart rate (HR), total cholesterol (TC), TG, high density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, fasting blood glucose (FBG), post-prandial 2 hour blood glucose (P2HBG), fasting blood insulin (FINS), and 2 hour post-prandial insulin (P2HINS) were measured before therapy and at the end of 3 months and 6 months. Insulin was measured at the same time by enzyme-linked immunosorbent assay (ELISA). Insulin sensitivity index homeostasis model assessment of insulin sensitivity (HOMA-IS) = $20 \times (\text{FINS}) / (\text{FBG} - 3.5)$; insulin resistance index homeostasis model assessment of insulin resistance (HOMA-IR) = $\text{FINS} \times \text{FBG} / 22.5$.

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Statistical analysis

Statistical analysis was performed by using the software SPSS 11.5 (SPSS Inc, Chicago, IL, USA). Insulin and insulin resistance index were of non-normal distribution, so we transformed them to a natural logarithm. All the data were presented as mean \pm SD. Parametric *t* tests were used to test differences between the two groups. A *P* level <0.05 was considered significant.

Results

All the patients completed the 6-month follow-up except 2 patients in the enalapril group; the reason was due to a cough.

The baseline data between the enalapril group and the telmisartan group in patients with hypertension as well as the results were listed in Table 1.

The effects on the blood pressure and heart rate

There was a significant reduction in the blood pressure in the telmisartan group after 3-month treatment ($P < 0.05$). There was no significant difference between the two groups in controlling blood pressure after 3-month treatment ($P > 0.05$). The blood pressure for the 6-month treatment did not decrease continually in the telmisartan group, and there was no significant difference between the two groups in blood pressure after 6-month treatment ($P > 0.05$). There was no significant difference between the two groups in heart rate before treatment and after treatment ($P > 0.05$).

The influence on blood lipid

The level of TG in the telmisartan group decreased obviously after 3-month treatment compared with that of pre-therapy and the enalapril group ($P < 0.05$), and the level of TG decreased more significantly after 6-month treatment ($P < 0.01$). The level of HDL cholesterol was significantly higher after 6-month treatment in the telmisartan group than that of pre-therapy and the enalapril group ($P < 0.05$).

The influence on blood glucose, FINS, HOMA-IS, and HOMA-IR

HOMA-IS and HOMA-IR in the telmisartan group were significantly lower than that of pre-therapy and of the enalapril group after 3-month treatment ($P < 0.05$). HOMA-IS, HOMA-IR, and P2HBG in the telmisartan group decreased significantly after 6-month treatment compared with pre-therapy and with the enalapril group ($P < 0.01$, $P < 0.01$, $P < 0.05$). HOMA-IS and HOMA-IR in the telmisartan group were lower after 6-month treatment than they were after 3-month treatment ($P < 0.05$).

Discussion

Hypertension is often accompanied by abnormal metabo-

lism of blood lipid and glucose. Antihypertensive medications have varying effects on blood lipid and insulin resistance. Although it is generally believed that angiotensin receptor blockers (ARBs) do not exert significant effects on carbohydrate and lipid metabolism, such views are based largely on the results of clinical trials and experimental studies that have been conducted with ARBs which are structurally quite different from telmisartan.

Benson et al. observed reductions in glucose, insulin, and triglyceride levels in telmisartan administered mice fed a diet rich in fat and carbohydrates.² Herein, our study focuses on the question whether telmisartan could lower blood lipid in hypertensive patients with dyslipidemia. Compared to the enalapril group, the telmisartan group had lower TG from (2.81 \pm 1.20) mmol/L to (2.40 \pm 0.81) mmol/L and were in the lower level 6 months later. However, it has no significant effect on TC and LDL cholesterol. In the enalapril group, we have not seen any changes in blood lipid including TG.

Today, there are many angiotensin ϕ receptor antagonists of which telmisartan is a new type. In our investigation, telmisartan can control blood pressure steadily. Some other trials demonstrated that it could reverse ventricular remodeling or hypertrophy and delay renal dysfunction just like the other ARBs.³ But there was no unanimous conclusion about whether telmisartan had a positive effect on blood glucose and lipid.⁴ We observed that it had a positive effect on TG and HDL cholesterol. Although it had no effect on the fasting blood glucose, telmisartan could reduce blood glucose after meals, insulin resistance, and could also increase insulin sensitivity; this is due to the fact that it is not only an ARB but also a PPAR γ which is expressed on lipid cells, and is thought to be an insulin sensitivity enhancer that can induce muscle to intake glucose mediated by insulin, lower free fatty acid (FFA) in lipid cells, improve lipid metabolism, lower TG and increase HDL cholesterol, and lessen inflammation and arteriosclerosis.^{5,6} So telmisartan can not only control blood pressure, but also improve glucose and lipid metabolism for patients with hypertension in combination with high blood lipid, especially with diabetes mellitus and obesity. There were no significant side effects observed in our investigation, and it was well tolerated and safe.

Takai et al. compared the protective effects of a highly lipophilic ARB, telmisartan, and an ARB with low lipophilicity, losartan, on vascular function and oxidative stress in stroke-prone spontaneously hypertensive rats.⁷ In that study, they concluded that telmisartan might be useful for preventing nicotinamide adenine dinucleotide phosphate (NADPH) oxidase activity, thereby conferring vascular protection.

Derosa et al. observed decreases in total cholesterol, LDL cholesterol, and triglyceride levels after 12 months of telmisartan treatment, as compared to eprosartan and placebo in their study of 119 hypertensive type 2 diabetes patients.⁸ However, our study demonstrated a neutral effect of telmisartan on plasma TC and LDL cholesterol levels. Perhaps it will require a longer treatment duration with telmisartan until the levels of TC and LDL cholesterol are lowered. In addition a

Table1 The comparison of blood pressure, heart rate, and biochemical data between the two groups ($\bar{x}\pm s$)

Variable	Telmisartan (n=46)			Enalapril (n=48)		
	Pre-therapy	3-month treatment	6-month treatment	Pre-therapy	3-month treatment	6-month treatment
SBP(mmHg)	149.24±5.02	136.30±4.70*	135.92±3.91	148.6±4.43	137.02±5.11	136.04±7.03
DSP(mmHg)	98.2±7.20	90.04±2.80*	88.10±3.03	99.12±2.97	89.31±3.01	87.23±4.12
HR (bpm)	72.13±5.41	71.12±4.61	71.01±5.01	73.04±5.90	0.23±4.82	72.10±3.69
TC(mmol/L)	6.12±1.92	6.04±0.702	5.80±0.83	6.14±1.0	6.01±1.11	5.94±1.09
TG(mmol/L)	2.81±1.20	40±0.81*	2.01±0.62**	2.78±1.08	2.73±0.92	2.62±1.10
LDL(mmol/L)	3.10±0.79	2.70±1.01	2.31±0.91	3.07±1.02	3.02±1.04	2.98±0.80
HDL(mmol/L)	1.40±0.72	1.49±0.94	1.65±0.90*	1.43±0.69	1.44±0.82	1.39±1.03
FBG(mmol/L)	4.50±0.48	4.61±0.51	4.63±0.55	4.60±0.51	4.71±0.49	4.73±0.54
P2HBG(mmol/L)	6.91±1.54	5.8±1.10	5.48±1.46*	7.01±1.48	6.43±1.38	6.70±1.41
FINS (mU/L)	0.901±0.25	0.871±0.41	0.88±0.34	0.8±0.43	0.87±0.50	0.85±0.32
P2HINS(mU/L)	2.12±0.25	2.01±0.38	0.96±0.43	2.1±0.31	2.03±0.42	1.99±0.45
HOMA-IR(mU/L)	0.25±0.26	0.28±0.48*	0.32±0.35**††	0.2±0.30	0.22±0.51	0.21±0.24
HOMA-IS(mU/L)	2.15±0.39	1.87±0.28*	1.60±0.32**††	2.1±0.28	2.01±0.31	2.02±0.26

* P<0.05 compared with pre-therapy and the enalapril group. ** P<0.01 compared with pre-therapy and the enalapril group. † P<0.05 compared with 3-month treatment.

larger group of patients would yield more conclusive results.

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