Acta Med. Nagasaki 50: 77－78

Case Report

Valsartan Suppresses an Increase in Urinary Catecholamines and Arrhythmias in a Patient with Hypertension

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We report a case of a 64-year-old woman with hypertension. She had dizziness and palpitation without heart failure although she was taking amlodipine. Urine levels of epinephrine and norepinephrine were high and both atrial and ventricular premature contraction were frequently seen. Valsartan, angiotensin II type 1 receptor antagonist, decreased these catecholamine levels and suppressed arrhythmias in the present case without the use of other drugs such as beta-blockers or anti-arrhythmic agents. In conclusion, valsartan is one option that can be used to prevent arrhythmias as well as to control blood pressure in hypertensive patients.

ACTA MEDICA NAGASAKIENSIA 50: 77－78, 2005

Keywords: Angiotensin II; Atrial premature contraction; Epinephrine; Norepinephrine; Ventricular premature contraction

Introduction

Essential hypertension goes along with sympathetic activation,[1] and sympathetic activation is related to arrhythmias.[2] Angiotensin-converting enzyme (ACE) inhibitor and the angiotensin II type 1 (AT1) receptor antagonist are one of the most popular anti-hypertensive agents. Moreover, it has been shown that these medicines have beneficial effects on arrhythmias in animal experiments.[3-5] However, there was no report about the effect of AT1 receptor antagonist on decrease of catecholamine and arrhythmias in hypertensive patients. We present a case of hypertension, medicated with calcium antagonist, whose urine level of catecholmines was normalized and arrhtymias were decreased by adding AT1 receptor antagonist to calcium antagonist.

Case report

A 64-year-old woman was admitted to the Department of Cardiovascular Medicine, Nagasaki University Hospital for assessment of dizziness and palpitation on October 26, 2002. She underwent the operation of mitral valvuloplasty in June 2001 because of severe mitral regurgitation due to mitral valve prolapse with congestive heart failure. After operation her condition was improved and amlodipine (5 mg), a calcium antagonist, was administered because of high blood pressure. However, the blood pressure changed sharply after the treatment, and she had dizziness and palpitation although she had no symptom of heart failure. On admission, her blood pressure was 150/96 mmHg, and pulse rate was 72/min. No significant heart murmur was heard. Chest X-ray and electrocardiogram were within normal limits. Echocardiogram revealed normal cavity size and normal wall motion of left ventricle (LV) and slight mitral regurgitation. The computed tomography (CT) showed no abnormality in the brain. Thyroid function, plasma levels of renin, aldosterone and cortizol were normal. Increased urine levels of epinephrine and norepinephrine were detected by measurements performed twice (Table 1). However, pheochromocytoma was denied by CT and iodine-131 metaiodobenzylguanidine schintigraphy. Holter electrocardiogram (ECG) and 24-h ambulatory blood pressure monitoring (24-h ABPM) with Holter ECG (Digital ECG and NIBP recorder FM-200, SCM-2000 system, Fukuda Denshi, Japan) were performed on October 30 and November 7, 2002, respectively. The number of ventricular premature contraction (VPC) measured on two days was 133 and 151, respectively and every VPC was single. The number of atrial premature contraction (APC) measured on two days was 7,372 and 4,851, respectively. Systolic blood pres-

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Received March 10, 2005; Accepted May 1, 2005

Table 1. Clinical examination findings and laboratory findings in the patient before and after valsartan administrationa

Variable	Date of measurement		
	October 30, 2002	November 7, 2002	December 3, 2002
Total heart beats (/day)	104,761	90,173	79,344
Heart rate (/min)	50-110	47-96	41-110
VPC counts (/day)[b]	151	133	17
APC counts (/day)[c]	7,372	4,851	148
Mean 24-h SBP/DBP (mmHg)[d]	NE[f]	129/80	116/71
Urine level of total catecholamine (μg/day)	189	205	95.4
Urine level of epinephrine (μg/day)	22.4	27.1	11.9
Urine level of noreepinephrine (μg/day)	166	177	83.4
Urine level of dopamine (μg/day)	557	596	555
Serum level of BNP (pg/mL)[e]	60	NE	55

[a]Administration of valsartan commenced on November 9, 2002.
[b]VPC=Ventricular premature contraction.
[c]APC=Atrial premature contraction.
[d]SBP=Systolic blood pressure; DBP=Diastolic blood pressure.
[e]BNP=Brain natriuretic peptide.
[f]NE=Not examined.

sure (SBP) was from 108 to 168 mmHg, diastolic blood pressure (DBP) was from 59 to 103 mmHg, and mean 24-h SBP/DBP was 129/80 mmHg. Then, from November 9, 2002, valsartan (40 mg), an angiotensin II type 1 antagonist, was administered with amlodipine once a day. About 4 weeks after the commencement of valsartan administration, VPC and APC were decreased in their number, blood pressure was normalized (SBP was from 84 to 117 mmHg; DBP was from 64 to 89 mmHg; and 24-h mean SBP/DBP was 116/71 mmHg), and urine levels of epinephrine and norepinephrine were also normalized (Table 1). Her symptoms disappeared. There was no noticiable change in serum level of brain natriuretic peptide (BNP) before and after valsartan administration.

Discussion

When valsartan administration attenuated urine levels of epinephrine and norepipephrine, arrhythmias were suppressed in the present case without the use of other drugs such as beta-blockers or anti-arrhythmic agents.

The arrhythmogenic properties of angiotensin II appear to be mediated by several mechanisms including its direct action on cardiac myocyte and stimulating the release of neurohumoral factors.[6] The previous reports demonstrated that angiotensin II potently enhanced catecholamine release from the sympathetic neurons,[7] atria,[8] and forearm.[9,10] Catecholamine exerts its own proarrhythmic effect on the heart as well as other pathophysiological consequences, such as the vasoconstricting and sodium-retaining properties of angiotensin II.[11]

Catecholamine is increased in chronic heart failure, and valsartan attenuated the plasma norepinephrine increase in the patients with chronic heart failure.[12] ACE inhibitor and AT1 receptor antagonist also prevent LV systolic and diastolic dysfunction as well as myocardial damage induced by excess beta-adrenergic stimulation.[13] The present case had no symptom of heart failure and normal LV function although serum level of brain natriuretic peptide (BNP) was slightly increased. Moreover, there was no significant change in serum level of BNP between before and after valsartan treatment. These suggest that valsartan suppresses an increase in catecholamine and may be related to a decrease in arrhythmia as well as control of hypertension in the present case.

Plasma renin and aldosterone levels were within normal limits in the present case. Maruyama et al.[5] mentioned that local angiotensin II production contributes to norepinephrine release and ventricular fibrillation via AT1-receptors in animal. Thus, local renin-angiotensin system may be important for catecholamine release and arrhythmia.

In conclusion, valsartan may be useful in reducing the risk of cardiovascular events by suppression of increased catecholamine and arrhythmias in hypertensive patients.

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