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Impact of telmisartan on coronary stenting in patients with acute myocardial infarction compared with enalapril

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Abstract

Objective: To determine whether telmisartan reduces in-stent restenosis (ISR) after coronary angioplasty using bare metal stent (BMS) in patients with acute myocardial infarction (AMI) compared with an angiotensin converting enzyme (ACE) inhibitor.
Background: The efficacy of inhibition of renin–angiotensin–aldosterone system in patients with AMI has been established, and the prescription of ACE inhibitor is recommended as class I indication for all AMI patients, whereas that of angiotensin II receptor blocker (ARB) as class IIa. Telmisartan is a unique ARB since it has a peroxisome proliferator-activated receptor (PPAR) gamma activating effect which is known to reduce neointimal tissue proliferation after coronary stenting.
Methods: In 64 patients, telmisartan (20–40 mg per day) was orally administered for 6 months after stenting (telmisartan group). The incidence of ISR after stenting in these patients was retrospectively compared with those in the other 60 patients administrated enalapril (2.5–5 mg per day) (enalapril group).
Results: There were no adverse events such as death, re-infarction and emergency bypass surgery in telmisartan group during a follow-up period for 6 months. The ISR rate was lower in telmisartan group (18.8%) than in enalapril group (33.3%) ($p=0.06$). However, percent diameter stenosis (%DS) at follow-up in telmisartan group was significantly smaller than in enalapril group (26.7±18.6% vs 38.0±23.9%, $p=0.004$). Late lumen loss was also significantly smaller in telmisartan group than in enalapril group (0.97±0.48 mm vs 1.19±0.68 mm, $p=0.039$).
Conclusions: Telmisartan not only is tolerable in patients with AMI but has a potential to reduce neointimal tissue proliferation after AMI treated with coronary angioplasty using BMS compared with enalapril.

Keywords: Telmisartan; In-stent restenosis; Acute myocardial infarction

1. Introduction

Although coronary stenting has been shown to reduce restenosis compared with balloon angioplasty, in-stent restenosis (ISR) remains a significant clinical problem, especially in patients with diabetes mellitus (DM) [1–5]. Drug-eluting stent (DES) has dramatically decreased ISR, but the use of DES for the patient with acute myocardial infarction (AMI) is still controversial. On the other hand, the efficacy of pharmacological inhibition of renin–angiotensin–aldosterone system in improving the prognosis of the patients with AMI has been established [6–9], and the prescription of angiotensin converting enzyme (ACE) inhibitor is recommended as class I indication for all AMI patients, while angiotensin II receptor blocker (ARB) as class IIa indication as an alternative to ACE inhibitor [10]. Several studies have suggested that tissue renin–angiotensin system also plays an important role in neointima formation. Angiotensin II not only induces vasoconstriction but also

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mediates vascular wall inflammatory responses as well as vascular smooth muscle proliferation [11]. ARBs have been shown to inhibit neointima formation after coronary stent implantation [15–17], whereas ACE inhibitors do not reduce the incidence of in-stent restenosis [27–30]. Telmisartan is a unique ARB with selective peroxisome proliferator-activated receptor (PPAR) gamma-modulating activity which is known to reduce neointimal tissue proliferation after coronary stenting. It is unknown whether such anti-proliferative effects after coronary stenting would be observed in telmisartan in AMI patients. The purpose of this study was to determine whether telmisartan can be tolerable in patients with AMI and can reduce ISR after coronary angioplasty using bare metal stent (BMS) in AMI patients compared with enalapril.

2. Methods

2.1. Patients

From January 2004 to August 2006, 403 patients with AMI were transferred to our institute, and underwent successful coronary angioplasty with the use of BMS. Two hundred and sixty-three (263 lesions) of them underwent follow-up catheterization at 6 months after the procedure. One hundred and twenty-four patients (124 lesions) of these 263 patients were administrated enalapril, the most common ACE inhibitor used in Japan, or telmisartan after stenting and were analyzed retrospectively. The administration of enalapril and telmisartan was not randomized, and enalapril was administered mostly to the patients administrated during the year of 2004, while telmisartan to those administrated after the year of 2005. The other 139 patients were not administrated enalapril or telmisartan because of severe liver or renal dysfunction or hypotension with systolic pressure <80 mm Hg in the hospital after stenting, or were administrated other ACE inhibitor or ARB, so that they were not included in this study. Diagnosis of AMI was performed by severe chest pain lasting >30 min, persistent ST segment elevation or depression on the ECG and abnormal rises of biochemical markers such as troponin T and the MB fraction of creatine kinase. All patients underwent baseline blood pressure, glucose level, and lipid level measurement at admission and at 6 months after the onset of AMI. Telmisartan group (64 patients) was treated with 20–40 mg per day of telmisartan. Enalapril group (60 patients) was treated with 2.5–5 mg per day of enalapril.

2.2. Stent implantation

In all patients, aspirin (200 mg) were orally administered just after admission to the emergency room, and 100 IU/kg heparin was administered intravenously at the beginning of the catheterization procedure. Activated coagulation time was maintained at >240 s throughout the stent implantation procedure by administering additional 1000 IU doses of heparin at an appropriate interval. None of the patients was pretreated with a thrombolytic agent and a glycoprotein IIb/IIIa inhibitor since the latter agent was not available in Japan. All stent implantation procedures were performed using a movable guide-wire (0.014-inch) and flexible balloon delivery system for predilatation. All patients underwent coronary stenting successfully with Driver stent (Medtronic AVE, Danvers, MA), Tsunami stent (Terumo, Tokyo, Japan), VISION stent (Guidant, Indianapolis, Ind), and Pixel stent (Guidant, Indianapolis, Ind). Directional coronary atherectomy or rotational atherectomy was not performed in any patients. All patients received 200 mg of aspirin, 200 mg of ticlopidine and 200 mg of cilostazol daily after stenting. Cilostazol was administrated for 3 days, ticlopidine for 4 weeks, and aspirin for a period as long as possible. Patients who could not be administrated ticlopidine due to its side effects were administrated cilostazol for at least 4 weeks instead of ticlopidine.

2.3. Angiographic analysis

Quantitative coronary angiography (QCA) was performed using an automated edge-detection system CMS (Medis Medical Imaging Systems, Nuenen, Netherlands) before and immediately after stenting, and at 6-month follow-up. A contrast-filled, non-tapered catheter tip was used for calibration. The reference vessel diameter (RVD), minimal lumen diameter (MLD), and percent diameter stenosis (%DS) were measured. Acute gain was defined as MLD immediately after the PCI procedure minus MLD before the procedure. Late lumen loss was defined as MLD immediately after the procedure minus MLD at follow-up. The measurements were done from the angiographies from multiple projections and the results from the "worst" views were recorded. Restenosis was defined as a diameter stenosis of 50% or more at follow-up angiograms. The analysis of QCA was made by the observers who were blinded to the patients treatment assignments.

2.4. Statistical analysis

All data are shown as mean ± one standard deviation. The differences in the continuous and categorized variables between the two groups were analyzed using the unpaired Student-*t* test and chi-square test, respectively. $p < 0.05$ was considered to be significant.

3. Results

Telmisartan or enalapril was initiated within 3 days after coronary stenting in all patients. No patient showed abnormalities in laboratory variables related to the administration of telmisartan or enalapril. One of the 60