Safety and Efficacy of Low-Dose Clopidogrel in Japanese Patients Undergoing Coronary Stenting
—— Preliminary 30-Day Clinical Outcome ——

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Background  A lower maintenance dose of clopidogrel may be appropriate in Japanese patients because the maintenance dose of ticlopidine is lower in Japan than that used in the United States.

Methods and Results  A total of 126 patients with 153 lesions who consented to take 50-mg clopidogrel to prevent stent thrombosis were enrolled. There was 1 case of early stent thrombosis (0.65%). Side-effects of clopidogrel occurred in 5 patients (4.0%).

Conclusion  This preliminary study shows that 50-mg clopidogrel may be acceptable in Japanese patients.

Key Words: Antiplatelet therapy; Stents; Stent thrombosis

The maintenance dose of ticlopidine is lower in Japan (100 mg twice daily) than that used in the United States (US) and Europe (250 mg twice daily).1,2 Thus a lower maintenance dose of clopidogrel may be appropriate for Japanese patients. The present study evaluated the safety and efficacy of low-dose (50 mg) clopidogrel in patients undergoing coronary stenting.

The Ethics Committee of Chiba University approved the study. Patients and the family were informed of (1) differences in the maintenance dose of ticlopidine for patients in Japan and those in the US and Europe, (2) the standard regimen after coronary stenting of clopidogrel plus aspirin that is used in almost all countries because of the better safety profile of clopidogrel, (3) the approval of 75-mg clopidogrel for Japanese patients with thrombotic stroke (and those undergoing coronary stenting for acute coronary syndrome from October 2007), (4) the use of 75-mg clopidogrel in the US and Europe, and (5) the potential risks and benefits of taking 50-mg clopidogrel. Patients were enrolled if both the patient and the family gave informed consent for taking 50-mg clopidogrel.

Between October 2006 and December 2007, 202 patients underwent successful coronary stent implantation and of them, 26 patients who had taken ticlopidine without any side-effects were excluded. Because there was not enough time to obtain informed consent, 42 patients who underwent emergency coronary angiography for acute myocardial infarction (MI) or unstable angina were excluded. Because of the preference of either the referring physician or the patient, 8 patients were excluded. Thus a total of 126 patients with 153 lesions were enrolled. Intravascular ultrasound (IVUS)-guided stenting was performed for all lesions. Aspirin (100 mg once daily) was used indefinitely. In all patients, 30-day clinical follow-up was available. The academic research consortium definitions of stent thrombosis were used.

Clinical assessment included evaluation of the side-effects of clopidogrel. Bleeding was defined as intracranial bleeding and hemorrhage with a decrease in hemoglobin ≥2 g/dl or blood transfusion. Blood testing was performed 2 and 4 weeks after stenting. Neutropenia was defined as neutrophil count <1.5×10⁹/L and use of granulocyte colony-stimulating factor. Thrombocytopenia was a platelet count <100×10⁹/L. Liver dysfunction was defined as an elevation of alanine transaminase (8–42 U/L), aspartate transaminase (13–33 U/L), alkaline phosphatase (115–359 U/L), or direct-bilirubin (≤0.4 mg/dl) of at least twice the upper normal value. Continuous and categorical variables are reported as mean±SD and number (%), respectively.

Patient, lesion, and procedural characteristics are shown in Table 1. There was 1 case of early stent thrombosis (0.65%), which resulted in acute MI and target lesion revascularization (TLR). During 30-day follow-up, no other patients had MI or TLR. There were no deaths. Side-effects of clopidogrel occurred in 5 patients (4.0%) (Table 2). We had already confirmed comparable antiplatelet effects for 50-mg clopidogrel and 200-mg ticlopidine. Recent studies have shown rates of early stent thrombosis of 0.5–0.8% in Japanese patients undergoing coronary stenting, which is comparable with the 0.65% found in the present study. IVUS-guided stenting may be partly associated with the low rate of early stent thrombosis, even while utilizing low-dose clopidogrel.

We previously reported a high incidence of side-effects of ticlopidine after drug-eluting stent (DES) implantation (9.3%).3 Within 30 days after the procedure, 3.2% of pa-
All further follow-up is mandatory to evaluate the safety and efficacy of the low-dose clopidogrel more than 30 days after DES implantation. However, based on the results of the present study, 50-mg clopidogrel may be used in patients undergoing BMS implantation. The sample size is relatively small and there was no control group. Most patients with acute MI were excluded, so the results may not be applicable to patients with acute MI or thrombus-containing lesions.

This preliminary study shows that 50-mg maintenance dose of clopidogrel may be acceptable in Japanese patients to prevent early stent thrombosis, at least in our hospital.

References