Efficacy of Cilostazol in Prevention of Bradycardia during Carotid Artery Stenting

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Background: Hypotension and bradycardia are known to occur frequently in carotid artery stenting (CAS), which may lead to postprocedural complications. The purpose of this retrospective study was to assess the efficacy of cilostazol, a phosphodiesterase 3 inhibitor, for preventing bradycardia and hypotension in the periprocedural period. *Methods:* The study population comprised 53 patients (54 lesions) with carotid artery stenosis who underwent CAS at our institution between 2004 and 2008. The patients were categorized by the use (group C, n = 26) or nonuse of cilostazol (group N, n = 28). The incidences of intraprocedural and postprocedural hypotension and bradycardia in each group were statistically assessed. *Results:* Intraprocedural hypotension and bradycardia occurred in 9 cases (34.6%) and 4 cases (15.3%) in group C and in 5 cases (17.9%) and 15 cases (53.6%) in group N, respectively. Postprocedural hypotension and bradycardia occurred in 4 cases (15.4%) and 0 cases in group C and in 1 case (3.6%) and 3 cases (10.7%) in group N, respectively. The incidence of intraprocedural bradycardia (IBc) was significantly lower in group C ($P = .0035$). Logistic regression analysis revealed that the use of cilostazol decreased the risk of IBc 99.5% (odds ratio [OR] = .01, 95% confidence interval [CI]: 5.46×10^{-6} to .04, $P = .001$) and distance from carotid bifurcation to maximum stenotic lesion was independently associated with IBc (OR = .46, 95% CI: .29-.74, $P = .001$). *Conclusion:* Use of cilostazol was associated with a lower incidence of IBc. Cilostazol may be a useful drug for the prevention of this complication. **Key Words:** Bradycardia—carotid artery stenting—cilostazol—hypotension.

Introduction

Carotid artery stenting (CAS) is indicated as an alternative to carotid endarterectomy for symptomatic patients at average or low risk of complications associated with endovascular intervention.[1] It is well recognized that hemodynamic instability (hypertension, hypotension, and bradycardia) often occurs after carotid endarterectomy, which may lead to postprocedural complications such as stroke or ischemic heart disease. Several risk factors, such as distance between bifurcation and maximum stenotic lesion, calcification at carotid bifurcation, and history of myocardial infarction,[2] have been documented. However, there are no reports regarding the relationship between preprocedural medication and hemodynamic instability in the periprocedural period for CAS. In this retrospective study, the efficacy of cilostazol for preventing bradycardia and hypotension during and after CAS was assessed.

Patients and Methods

Between January 2004 and March 2008, 53 patients (54 lesions) with carotid artery stenosis underwent CAS.

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The average age was 72.3 (59-86), and 49 were men. All patients received dual antiplatelet therapy (DAPT) before the procedure. The combination of drugs for DAPT was decided in the following manner: (1) for patients who had already received DAPT before referral, their prescription was continued (aspirin 100mg and cilostazol 200mg daily: 14 cases, aspirin 100mg and ticlopidine 200mg: 17 cases, aspirin 100mg and clopidogrel 75mg: 2 cases), (2) for patients who only received aspirin 100mg at the time of referral, cilostazol 200mg (12 cases) was added until 2006, and clopidogrel 75mg (5 cases) was used thereafter as an adjuvant, and (3) for patients who only received ticlopidine 200mg (3 cases) or clopidogrel 75mg (1 case) at the time of referral, aspirin 100mg was added before the procedure. DAPT was continued for at least 3 months postoperatively, followed by a single antiplatelet therapy with aspirin for another 3 months in most case. In some cases with prior coronary artery disease and/or peripheral artery disease, DAPT was continued if necessary.

For the assessment of carotid artery plaque, preoperative carotid artery magnetic resonance imaging using 3-dimensional inversion-recovery–based T1-weighted imaging (magnetization-prepared rapid acquisition gradient-echo [MPRAGE][3]) was performed. The signal intensity of the carotid artery plaque on MPRAGE sequences was classified as "high" when the intensity was more than 200% that of the adjacent muscle.

Procedure

An 8F guiding catheter was introduced via the femoral artery. During the procedure, heparin was intra-arterially and intravenously administered to achieve an activated clotting time of more than 250 seconds. In all, .25 mg of atropine sulfate was administered before predilatation for prophylaxis to prevent bradycardia and hypotension. PercuSurge balloon catheter (Medtronic, Inc., Minneapolis, MN) was used as a device to protect against distal embolism. Predilatation was performed with a balloon catheter (3.5-4.0 mm). A self-expandable stent with a small-cell design was used for the stenting. Stents used in this series were PRECISE (Cordis Endovascular, Miami Lakes, FL) in 29 patients, SMARTeR (Cordis Endovascular, Miami Lakes, FL) in 15 patients, PROTÈGÈ (ev3, Inc., Plymouth, MN) in 5 patients, XPert (Abbott Vascular, Santa Clara, CA) in 2 patients, Wallstent (Boston Scientific Corporation, Natick, MA) in 1 patient, PENTA (Abbott Vascular, Santa Clara, CA) in 1 patient, and Multilink Zeta (Abbott Vascular, Santa Clara, CA) in 1 patient. In cases in which more than 50% remaining stenosis according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria was observed after stenting, postdilatation was performed. If residual stenosis was less than 50% or the plaque was vulnerable, which was defined as a high-intensity lesion detected by MPRAGE, postdilatation was not carried out. The definitions of bradycardia and hypotension were 50 beats per minute and less than 90 mm Hg (systolic blood pressure), respectively. In cases of intraprocedural bradycardia (IBc), .25-.50 mg of atropine sulfate was used, and in intraprocedural hypotension (IHo), 1-4 mg of etilefrine was administered.

Patients were divided into 2 groups: those who were prescribed cilostazol (group C, n = 26) and those who were not (group N, n = 28). Changes of blood pressure and heart rate were measured via an invasive arterial catheter in the radial artery and an electrocardiogram monitor during and after the procedure.

Statistical Analyses

All statistical analyses were performed using JMP version 9.0 (SAS Institute, Cary, NC) and STATA version 11(STATA Corp, College Station, TX). Values are presented as the mean ± SD. Categorical variables were compared by Fisher exact probability test. Continuous variables with normal distributions were analyzed by Student t test and those with non-normal distributions were analyzed by the Mann–Whitney U test. The incidences of intraprocedural and postprocedural bradycardia and hypotension were calculated, and statistical analyses were performed among subgroups sorted by the use or nonuse of cilostazol. Furthermore, IBc was tested using age, sex, distance from carotid bifurcation to maximum stenotic lesion, side of the lesion, history of coronary artery disease, postdilatation, calcification at the carotid bifurcation, and cilostazol using univariate and multivariate analyses by logistic regression. Stepwise logistic regression with backward elimination was used to select the most significant predictors. Statistical significance was defined as a P value less than .05.

Results

Successful dilation of the carotid lesion was obtained in all patients. Temporary transcutaneous pacing was not used in this study. Also, we did not experience hazardous complication, such as cardiac failure, which was considered to be the side effect of colostazol in this series. No hemorrhagic complications were observed in this series. Ischemic complications occurred in 1 case in group C and in 1 case in group N. There was no significant difference in the incidence of ischemic complications among the groups.

The characteristics of the patients in each group are summarized in Table 1. Demographic data, risk factors, population with symptomatic stenosis, degree of stenosis, MPRAGE signal intensity, and calcification at the carotid bifurcation were similar between the groups. There were significant differences in side of lesion (61.5% versus 32.1%; $P = .029$), distance from carotid bifurcation to maximum stenotic lesion (4.5 ± 3.9 versus 9.5 ± 5.0; $P < .001$), and application of postdilatation (23.1% versus 50.0%; $P = .038$). There were no significant differences in