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Research Article

Preventive Effect of Cilostazol on Bradycardia Attacks during Carotid Angioplasty with Stenting

Nozomu Kobayashi*

Stroke Center, Kainan Hospital, Aichi Prefectural Welfare Federation of Agricultural Cooperatives, Japan

Abstract

This study was performed to evaluate the preventive effect of cilostazol on bradycardia attacks during the carotid angioplasty with stenting (CAS) procedure. Among the 38 CAS procedures performed by the first author between April 2004 and May 2008, we analyzed 18 cases in which a hypotension attack occurred during the procedure. Of the 18 patients valuated, 9 received cilostazol before the procedure (Cil (+) group), and the remaining 9 did not (Cil (-) group). In all procedures, 0.5mg of atropine was administered just before stent placement or balloon inflation. If a hypotension attack occurred, intravenous fluid loading or vasopressors such as ephedrine or catecholamine were used. A hypotension attack in this study was defined as the need for special treatment for low blood pressure. Pre-procedural heart rate (HR) was significantly higher in the of Cil (+) group than in the Cil (-) group (mean HR: 95.0 vs. 77.6, P<0.01). Intra-procedural minimum HR was significantly higher in the Cil (+) group than in the Cil (-) group (mean HR: 90.1 vs. 67.8, P<0.01). A statistically significant change in HR from pre-procedural HR to the minimum intra-procedural HR was observed in the Cil (-) group. Whereas the difference did not reach statistical significance in the Cil (+) group. Pre-procedural administration of cilostazol is an easy and useful method for the prevention of bradycardia attacks during the CAS procedure.

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Ischemic Stroke: A Cerebrovascular Accident

***Corresponding author**

Nozomu Kobayashi, Stroke Center, Aichi Prefectural Welfare Federation of Agricultural Cooperatives, 396, Maegasucho, Yatomi, Aichi, Japan, 498-0017, Tel: +81-567-65-251; Fax: +81-567-67-3697; E-mail: cbk71850@pop06.odn.ne.jp

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- Antiplatelet agents
- Bradycardia
- Carotid artery stenosis
- Stents

ABBREVIATIONS

AS: Carotid Angioplasty with Stenting; **CEA:** Carotid-endoarterectomy; **HR:** Heart Rate

INTRODUCTION

Carotid angioplasty with stenting (CAS) has been recognized as a useful modality for the treatment of severe carotid stenosis similar to carotid-endoarterectomy (CEA) [1]. Despite its therapeutic value, CAS has been associated with intraprocedural complications such as hypotension and bradycardia [2]. Cilostazol, a cyclic adenosine monophosphate phosphodiesterase inhibitor that is widely used as an anti-platelet drug for ischemic stroke prevention [3] in Japan, may induce tachycardia [4] and is used for the treatment of bradycardia [4-6].

In the present report, we discuss the preventive effect of cilostazol on bradycardia attacks during the CAS procedure.

MATERIALS AND METHODS

Among the 38 CAS procedures performed by the first author between April 2004 and May 2008, we analyzed 18 cases in which a hypotension attack occurred during the procedure. All of the patients had primary lesions without a previous history of CAS or CEA. A hypotension attack was defined as the need for special treatment for low blood pressure. All CAS procedures were successfully performed using self-expandable stents with specific protection methods. The types of stents used included SMART (Johnson and Johnson, New Jersey), Precise ((Johnson and Johnson, New Jersey), and Wallstent (Boston Scientific, Massachusetts) (Table 1). In all the cases, dual antiplatelet therapy was administered before and after the procedure. Anti-platelet agents were selected from ticlopidine, clopidogrel, aspirin, and cilostazol, which can be used officially for stroke prevention in Japan. Therapeutic agents were selected based on previous treatment by the family physician. Patients receiving single anti-platelet therapy were treated with supplementary clopidogrel or aspirin at least 4days before the procedure.

Of the 18 patients valuated, 9 received cilostazol before the procedure (Cil (+) group), and the remaining 9 did not (Cil (-)

group). The patients' data are listed in Table 1. No statistically significant differences were observed between the two groups regarding age, sex, stenotic rate, stent used, and drugs administered to treat hypotension attacks during the operation.

During the procedure, systemic heparinization was performed to maintain the activated-clotting-time at >280 seconds. In addition, 0.5mg of atropine was administered just before stent placement or balloon inflation to reduce the risk of bradycardia or hypotension. Continuous electrocardiography and continuous blood pressure monitoring with an automatic cuff attached to the patient's arm were performed throughout the procedure. If a hypotension attack occurred, intravenous fluid loading or vasopressors such as ephedrine or catecholamine were used. Pre-procedural heart rate (HR), intra-procedural minimum HR and HR alterations during the procedure were retrospectively analyzed and compared between the Cil (+) and Cil (-) groups.

Statistical analyses were performed using the Mann-Whitney *U* test and Wilcoxon signed-rank test on the statistical software Stat-View.

RESULTS

Pre-procedural HR was significantly higher in the of Cil (+) group than in the Cil (-) group (mean HR: 95.0 vs. 77.6, P<0.01; Figure 1). Intra-procedural minimum HR was significantly higher in the Cil (+) group than in the Cil (-) group (mean HR: 90.1 vs. 67.8, P<0.01; Figure 2). A statistically significant change in HR from pre-procedural HR to the minimum intra-procedural HR was observed in the Cil (-) group (Figure 3). Whereas the difference did not reach statistical significance in the Cil (+) group (Figure 4).

DISCUSSION

Currently, CAS is widely accepted as a treatment option for severe carotid artery stenosis [1]. In the CAS procedure, the administration of multiple oral anti-platelet drugs is recommended [1]. Cilostazol is an antiplatelet agent that is used for the prevention of cerebral infarction in Japan and is, therefore, an option as an antiplatelet drug for use during the CAS procedure.

Table 1: Patient data in former period.

	Cil(+)	Cil(-)	p value
Age(y.o.)	56~86(mean 73.7)	56~88(mean 71.0)	N.S.
Gender(male/female)	9/0	9/0	N.S.
Stenotic rate(NASCET%)	60~97(mean 74.7)	65~90(mean 78.7)	N.S.
Past histry of coronary artery disease			
Stent			
SMART/PRECISE	7	8	N.S.
WALL	2	1	
Corresponds for hypotention attack			
volume load	2	3	N.S.
vasopressor*	7	6	

Abbreviations: N.S.: not significant.
*"vasopressor" includes ephedrine and cathecolamine.

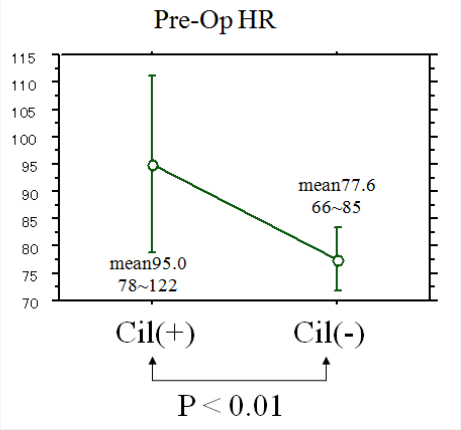

Figure 1 Pre-procedural HR was significantly higher in the of Cil(+) group than in the Cil(-) group (mean HR: 95.0 vs. 77.6, P<0.01).

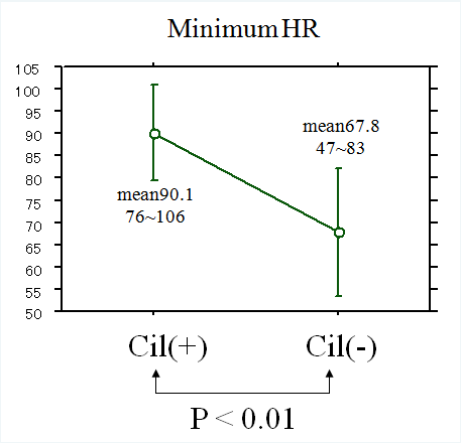

Figure 2 Intra-procedural minimum HR was significantly higher in the Cil(+) group than in the Cil(-) group (mean HR: 90.1 vs. 67.8, P<0.01).

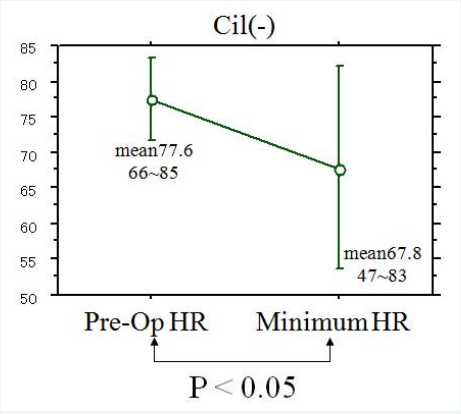

Figure 3 A statistically significant change in HR from pre-procedural HR to the minimum intra-procedural HR was observed in the Cil(-) group.

Cilostazol increases cyclic adenosine monophosphate levels via inhibition of cyclic adenosine monophosphate phosphodiesterase [7]. It has antithrombotic effects and is useful for stroke prevention [3] and for the treatment of chronic peripheral arterial occlusive disease [8]. It has other chronotropic

effects such as vasodilation and inhibition of smooth muscle cell proliferation [7]. In addition, it is known to have cardiotonic effects [7]. Therefore, cilostazol has been reported to be useful for the treatment of bradyarrhythmias [4-6].

During the CAS procedure, vital signs may become unstable [2]. Bradycardia is less common than hypotension [2] and could be avoided to some extent by prophylactic atropine administration [9]. However, such hemodynamic instability is not always benign [2] and may induce cardiac morbidity [9]. Therefore, it is still an important problem associated with CAS procedure.

In the present study, we showed that despite the occurrence of vital sign instability such as hypotension during CAS procedure requiring specific treatment, the patients treated with cilostazol showed relatively mild bradycardia attacks (Figure 2). One possible reason for this is Cil (+) group showed a higher mean HR in the pre-procedural period (Figure 1) because of the tachycardia induced by cilostazol administration. However, the difference between the pre-procedural HR and the intra-procedural minimum HR was significantly smaller in the Cil (+) group than in th Cil (-) group (Figure 3 and 4). The change in HR was statistically significant in the Cil (-) group, but not in the Cil (+) group. Considering these results, cilostazol appears to have preventive effect on HR reduction during the CAS procedure, independent from the induction of tachycardia.

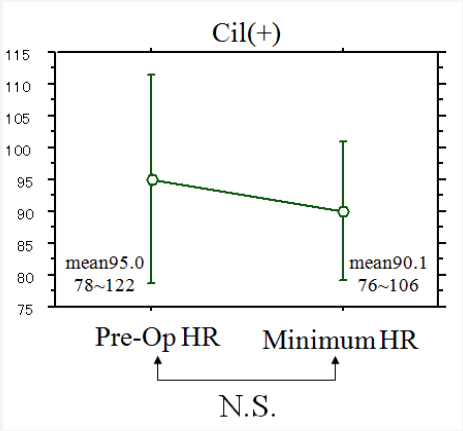

Figure 4 A change in HR from pre-procedural HR to the minimum intra-procedural HR was not significantly different in the Cil(+) group.

In addition, cilostazol has been reported to reduce restenosis after CAS [10]. Therefore, cilostazol is a useful and promising agent for CAS procedures.

CONCLUSION

Pre-procedural administration of cilostazol is an easy and useful method for the prevention of bradycardia attacks during the CAS procedure.

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