Relation between the Incidence of Arrhythmias and Ischemic ST-Segment Depression during Dipyridamole Electrocardiography Test in Patients with Coronary Artery Disease

Takehiko Shibata, M.D., Isao Kubota, M.D., Kozue Ikeda, M.D., Michiyasu Yamaaki, M.D., Kanji Hanashima, M.D., Kai Tsuki, M.D., and Shoji Yasui, M.D.*

Summary

To examine the incidence of arrhythmias in dipyridamole infusion and the relation between dipyridamole-induced arrhythmias and ST-segment depression, dipyridamole electrocardiography tests were performed on 100 patients with coronary artery disease. Dipyridamole was infused at a rate of 0.568 mg/kg for 4 min, and 87-lead body surface mapping was performed to determine ischemic ST-segment depression. Positive ischemic response was defined as ≥0.10 mV horizontal or downsloping ST-segment depression below the baseline, lasting 80 msec after the J point. Arrhythmias were observed by continuous electrocardiographic monitoring using a CM-5 lead electrocardiography. With respect to ventricular premature contractions (VPC), a group of patients with previous myocardial infarction (MI group) had a significantly higher incidence than a group of patients without previous myocardial infarction (non-MI group) before (16.7% vs. 1.7%, p<0.01) and after (38.1% vs. 3.4%, p<0.005) the dipyridamole infusion. The incidence of supraventricular premature contractions (SVPC), however, was not significantly different between the MI and non-MI groups. A group of patients with positive ischemic response had a significantly higher incidence of SVPC after the dipyridamole infusion than a group of patients with negative ischemic response (p<0.005). However, there was no significant difference in the incidence of VPC between the negative and positive ischemic response groups. These results suggest that dipyridamole-induced VPC is not always associated with ischemic ST-segment depression, but dipyridamole-induced SVPC is associated with dipyridamole-induced ischemic ST-segment depression in patients with coronary artery disease.
It is believed that dipyridamole infusion induces myocardial ischemia, and the dipyridamole infusion test is used clinically as a reliable method for the detection of coronary artery disease (CAD).1)-12) Although the dipyridamole infusion test is now in common use, there have been few studies of the incidence of dipyridamole-induced arrhythmias in patients with CAD.7),8) In this study, the incidence of arrhythmias in the dipyridamole infusion test was investigated separately in patients with previous myocardial infarction (MI) and in those without MI. Additionally, we investigated the relation between the incidence of arrhythmias and ischemic ST-segment depression seen during dipyridamole electrocardiography testing.

**METHODS**

**Subjects**

One hundred patients (82 men and 18 women, ages 35–73 years, mean ±SD 58±8 years) with CAD were studied. The 100 patients with CAD consisted of 58 patients without previous myocardial infarction (non-MI group) and 42 patients with previous myocardial infarction (MI group). The 42 patients with previous myocardial infarction (MI) had a documented transmural myocardial infarction that was more than 4 weeks old. None had bundle branch block or intraventricular conduction disturbances on electrocardiograms (ECGs).

Informed consent was obtained from each subject before entering the study. The study protocol was approved by the Ethical Committee on Clinical Research of Yamagata University.

**Dipyridamole electrocardiography test**

Dipyridamole was infused intravenously at a dose of 0.568 mg/kg for 4 min1)-7) into the antecubital vein. All subjects were kept relaxed in the supine position at the time of recording.

Continuous ECG monitoring and recordings were performed using a CM-5 lead ECG in the 10-min period before infusion and for 20 min after the beginning of infusion.

Body surface electrocardiographic mapping was performed using a HPM-5100 system (Chunichi Denshi Corporation, Nagoya, Japan)4)-6),9),13)-15) or VCM-3000 system (Fukuda Denshi Corporation, Tokyo, Japan)16)-18)
Eighty-seven electrodes were placed over the torso (59 leads on the anterior chest and 28 on the back).4)-6),9),13)-18) The 87-lead ECGs were sampled simultaneously, using Wilson’s central terminal as a reference, at a rate of 250 samples/sec (HPM-5100) or 1,000 samples/sec (VCM-3000). The 87-lead body surface ECG data were recorded just before and at 5, 10, 15, and 20 min after the beginning of infusion.

ST-segment depression was examined using the 87-lead ECGs. A positive ischemic response was defined as ≥0.10 mV horizontal or downsloping ST-segment depression below the baseline, lasting 80 msec after the J point.

Aminophylline (125–250 mg), which specifically blocks the vasodilating action of dipyridamole,19) was administered intravenously when the subjects experienced moderate or severe angina with ischemic ST-segment depression or clinical side effects.

To eliminate other drug effects, all medications were withheld for at least 24 hours before the dipyridamole electrocardiography test.

**Arrhythmias**

We examined arrhythmias in a 10-min pretreatment period (before), a 4-min period during infusion (during), and a 10-min period after the end of infusion (after). The arrhythmias observed in testing were ventricular premature contractions (VPC) and supraventricular premature contractions (SVPC). In the present study, we studied only VPC and SVPC judged by 3 physicians.

**Statistical analysis**

Data on each patient were analyzed at the Yamagata University Computer with SAS (Statistical Analysis System). The results were expressed as mean±SD (standard deviation). Statistical analyses of incidence of arrhythmias were evaluated using the chi-square test. A p value <0.01 was considered significant.

**Results**

In this study, arrhythmias observed in the dipyridamole infusion were isolated VPC or SVPC. Ventricular or supraventricular beats in consecutive runs of two or more were not observed.

Figure 1 shows the incidence of arrhythmias in non-MI and MI groups. The incidence of VPC in the MI group was significantly higher than that in the non-MI group before (p<0.01) and after (p<0.005) dipyridamole infusion. However, the incidence of SVPC was not significantly different be-
The incidence of VPC in a MI group was significantly higher than that of a non-MI group before (p<0.01) and after (p<0.005) dipyridamole infusion. However, the incidence of SVPC was not significantly different between the 2 groups. VPC=ventricular premature contraction; SVPC=supraventricular premature contraction; MI=previous myocardial infarction.

tween the 2 groups. The incidences of VPC and SVPC before and after dipyridamole infusion were compared with each other. The incidence of VPC in the MI group and the incidence of SVPC in the non-MI group after the dipyridamole infusion were significantly higher than those before the dipyridamole infusion (p<0.05 and p<0.005, respectively). On the other hand, the incidence of VPC in the non-MI group and the incidence of SVPC in the MI group after the dipyridamole infusion were not significantly higher than those before the dipyridamole infusion. The incidence of positive ischemic response of the non-MI group was significantly higher than that of the MI group (46.6% vs. 19.0%, p<0.005, respectively).

Figure 2 shows the incidence of arrhythmias in patients with coronary artery disease based on negative or positive ischemic response. There was no significant difference in the incidence of VPC between the 2 groups. On the other hand, the incidence of SVPC after the dipyridamole infusion for the positive ischemic response group was significantly higher than that for the negative ischemic response group (p<0.005). However, there were no significant differences between the 2 groups in the incidence of SVPC before and during the dipyridamole infusion.
Fig. 2. Incidence of arrhythmias in patients with coronary artery disease based on negative or positive ischemic response. There were no significant differences in the incidence of VPC between the 2 groups. On the other hand, the incidence of SVPC after dipyridamole infusion for the positive ischemic response group was significantly higher than that for the negative ischemic response group (p<0.005). However, there were no significant differences between the 2 groups in the incidence of SVPC before and during dipyridamole infusion. VPC=ventricular premature contraction; SVPC=supraventricular premature contraction; Neg=negative ischemic response; Pos=positive ischemic response; NS=not significant.

Discussion

Intravenous dipyridamole has been reported to provoke angina and myocardial ischemia because of its coronary vasodilative effect. Therefore, the dipyridamole infusion test has recently become widely used for the diagnosis of CAD. Some investigators have reported that cardiac arrhythmias do not occur in the dipyridamole infusion. However, detailed information about the occurrence of dipyridamole-induced arrhythmias in relation to ischemic response or myocardial infarction is not known. The purpose of this study was 1) to examine the incidence of arrhythmias in the dipyridamole infusion, and 2) to investigate the relation between dipyridamole-induced arrhythmias and ischemic ST-segment depression in the dipyridamole electrocardiography test.

Dipyridamole-induced ventricular premature contraction

Goldshlager et al have reported that myocardial ischemia is one of
The causes of exercise-induced VPC in patients with CAD. On the other hand, it has been reported that the infusion of dipyridamole induces myocardial ischemia in patients with CAD.\(^3\)-\(^6\),\(^9\),\(^11\),\(^12\) If dipyridamole induces ischemia, it may also induce VPC. Concerning the incidence of VPC and ischemic response (Fig. 2), the positive group for ischemic response did not have a significantly higher incidence than the negative group. These results suggest that the dipyridamole-induced VPC is not always associated with myocardial ischemia. In this study, the incidence of VPC in the MI group was significantly higher than that of the non-MI group before (p<0.01) and after (p<0.005) dipyridamole infusion (Fig. 1). It is thought that the higher incidence of VPC in the MI group (Fig. 1) may be associated with wall motion abnormalities or left ventricular dysfunction.\(^2\),\(^3\)

**Dipyridamole-induced supraventricular premature contraction**

To our knowledge, few previous studies\(^7\) have reported the incidence of SVPC in dipyridamole infusion. In this study, there was no significant difference between the MI and non-MI groups in the incidence of SVPC in the dipyridamole infusion. However, the incidence of SVPC in the non-MI group tended to be higher than that in the MI group (Fig. 1). In Fig. 2, the positive ischemic response group had a higher incidence of SVPC after dipyridamole infusion than the negative ischemic response group (p<0.005). These results suggest that the dipyridamole-induced SVPC may be associated with myocardial ischemia. However, the precise mechanism of the dipyridamole-induced SVPC remains unknown and further investigation will be necessary.

**Limitations**

In this study, ischemic ST-segment depression in the dipyridamole electrocardiography test was considered to be a positive ischemic response indicating myocardial ischemia. However, ischemic ST-segment depression does not always reflect myocardial ischemia. Thus, the dipyridamole-induced arrhythmias are related to ischemic ST-segment depression, but not always to myocardial ischemia.

**Conclusion**

We evaluated the incidence of dipyridamole-induced arrhythmias in patients with CAD. It was demonstrated that dipyridamole-induced VPC is not always associated with ischemic ST-segment depression, but that dipyridamole-induced SVPC is associated with ischemic ST-segment depression in patients with CAD.
REFERENCES


