
The Association of Dipyridamole Side Effects with Hemodynamic Parameters, ECG Findings, and Scintigraphy Outcomes

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Dipyridamole has extensively been administered as a substitute for physical activity in cardiovascular assessment. The aim of this study was to evaluate the association of dipyridamole side effects with hemodynamic oscillations, scanning results, and electrocardiography (ECG) findings. **Methods:** Overall, 590 patients referred to the nuclear medicine center for myocardial perfusion imaging were evaluated for adverse dipyridamole effects concurrent with a low level of exercise. Before and during dipyridamole infusion, the patients' vital signs, electrocardiogram, heart rate, systolic blood pressure, and diastolic blood pressure were monitored; all patients underwent stress-rest ^{99m}Tc-sestamibi gated SPECT using a 2-d protocol. **Results:** Eighty-eight patients (14.9%) experienced at least one side effect during dipyridamole infusion, and abnormal ECG and scan results were observed in 32.4% and 48.6% of patients, respectively. We observed a positive correlation between a higher incidence of chest discomfort, headache, and dyspnea and abnormalities on ECG and myocardial perfusion imaging. In addition, these 3 side effects were also associated with a higher postinfusion heart rate, lower preinfusion systolic blood pressure, and lower postinfusion diastolic blood pressure. There were significant differences between pre- and postinfusion heart rate, preinfusion systolic blood pressure, and postinfusion diastolic blood pressure among patients with or without side effects, whereas no significant difference was observed in any of the hemodynamic parameters between patients with normal and abnormal ECG results or myocardial perfusion imaging results. **Conclusion:** This study demonstrated a correlation between hemodynamic variables and side effects but not with imaging findings or ECG findings.

Key Words: dipyridamole; hemodynamic changes; myocardial SPECT; ECG

J Nucl Med Technol 2010; 38:149–152

DOI: 10.2967/jnmt.109.072629

The administration of dipyridamole during perfusion scintigraphy has extensively been applied to simulate the effects of physical activity in patients who are incapable of performing a conventional exercise test (1–3). The addition of a symptom-limited exercise test is also considered safe and efficient. Compared with dipyridamole infusion alone, exercise added to dipyridamole infusion has been shown to result in fewer noncardiac side effects, the same prevalence of angina pectoris, and a higher incidence of ST segment changes (4).

Dipyridamole, by itself, can cause hypotension, dyspnea, dizziness, and electrocardiography (ECG) abnormalities; however, simultaneous dipyridamole administration and scanning should be treated as a distinct situation and demands its own risk assessment. Several studies have evaluated the safety and diagnostic precision of dipyridamole–thallium imaging in subjects with suspected coronary artery disease (5,6).

The purpose of this study was to assess the incidence of dipyridamole side effects and their association with hemodynamic changes, scanning results, and ECG findings.

MATERIALS AND METHODS

Participants and Study Design

Overall, 590 patients (mean age \pm SD, 57 \pm 11 y) who underwent myocardial perfusion scanning with intravenous dipyridamole in the stress phase for detection of possible coronary artery disease were assessed in a prospective study. The patients fasted overnight, and all cardiovascular medications were discontinued at least 2 d before the study. The ECG, blood pressure, heart rate, systolic blood pressure, and diastolic blood pressure of all patients were determined both before and after dipyridamole administration. Infusion of dipyridamole (0.568 mg/kg) was followed by a low level of exercise (60 rpm/30 W) for 3 min to attain maximal coronary blood flow and to reduce radionuclide uptake in the gastrointestinal organs (4). Four minutes later,

Received Nov. 9, 2009; revision accepted Mar. 29, 2010.

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^{99m}Tc -sestamibi (740 MBq) was administered parenterally and imaging was performed 90 min after the initial infusion of dipyridamole; the rest-phase examination was performed on the following day. An abnormal ECG was designated as one showing a 0.1-mV horizontal or downsloping ST segment depression of 80 ms after the J point.

Acquisition Protocol

All patients underwent stress–rest ^{99m}Tc -sestamibi gated SPECT using a 2-d protocol. Rest gated SPECT was performed 90 min after intravenous injection of 740 MBq of ^{99m}Tc -sestamibi. SPECT was performed with the patient supine. We used a dual-head γ -camera in the 90° setting (DLXi; GE Healthcare), equipped with high-resolution, low-energy collimators. Sixty-four views over 180° were obtained from 45° right anterior oblique to 45° left posterior oblique. Images were acquired for 25 s per view with a zoom factor of 1.45, were gated at 8 frames per cardiac cycle using an R-wave trigger, and were stored in a 64 × 64 matrix. The gated short-axis images were then processed for automatic left ventricular ejection fraction quantification using MultiDim quantitative gated SPECT software (Stanford University).

The study was approved by the institutional ethics committee of Golestan University of Medical Science and complied with the tenets of the Declaration of Helsinki; all patients gave written informed consent.

Statistical Analysis

The data are represented as mean \pm SD; to compare quantitative variables between groups, we used either the *t* test or the paired *t* test; the χ^2 test was also applied to analyze nonparametric data; a *P* value of less than 0.05 was considered to be statistically significant.

RESULTS

Overall, 88 patients (14.9%) experienced at least one undesirable side effect during dipyridamole infusion; among which chest discomfort (5.2%) stands as the most frequent complaint (Table 1); an abnormal ECG and irregular scan findings were observed in 191 (32.4%) and 287 (48.6%) patients, respectively. Patients with abnormal ECG findings had a remarkably higher incidence of side effects than did patients with normal ECG findings (32.9% vs. 6.2%; *P* < 0.05). The same findings were also observed when we compared the data of patients with abnormal scans to those with normal scans (22.6% vs. 7.5%; *P* < 0.05). The ejection fraction was 57% \pm 12% in the stress phase and 59% \pm 11% on rest-phase gated images. A higher incidence of chest discomfort, headache, and dyspnea correlated positively with abnormal findings on the ECG and myocardial perfusion images. In addition, these 3 side effects were associated with a higher postinfusion heart rate, lower preinfusion systolic blood pressure, and lower postinfusion diastolic blood pressure.

Dipyridamole administration resulted in a rise in heart rate (82 \pm 12 vs. 89 \pm 13 beats/min) and systolic blood

TABLE 1
Frequency of Various Side Effects in Patients

Side Effect	<i>n</i>
Chest discomfort	31 (5.2%)
Dizziness	5 (0.8%)
Dyspnea	18 (3%)
Flushing	6 (1%)
Headache	15 (2.5%)
Nausea	3 (0.5%)
Palpitation	3 (0.5%)
Sweating	4 (0.6%)
Ventricular tachycardia	1 (0.1%)
Vomiting	2 (0.3%)
Total	88 (14.9%)

pressure (138 \pm 20 vs. 132 \pm 21 mm Hg) and a fall in diastolic blood pressure (79 \pm 8 vs. 75 \pm 9 mm Hg) (*P* < 0.001). Comparing the data of patients who experienced at least one side effect with those who had no side effects, we found a significantly higher postinfusion heart rate (82 \pm 13 vs. 92 \pm 10 beats/min; *P* = 0.016), a lower preinfusion systolic blood pressure (139 \pm 20 vs. 133 \pm 23 mm Hg; *P* = 0.024), and a lower postinfusion diastolic blood pressure (76 \pm 9 vs. 72 \pm 10 mm Hg; *P* = 0.003) in patients who had side effects. However, there were no noticeable alterations in resting heart rate, preinfusion diastolic blood pressure, and postinfusion systolic blood pressure (*P* > 0.05) (Table 2).

No significant difference was observed in any of the hemodynamic parameters when patients with an abnormal ECG were compared with those with normal ECG findings; the same results were also obtained between normal and abnormal myocardial perfusion imaging groups (*P* > 0.05) (Table 2).

DISCUSSION

Intravenous dipyridamole administration during perfusion scintigraphy is applied as an alternative to exercise for coronary artery disease detection and risk assessment in clinical practice. Dipyridamole enhances left ventricular ejection fraction and heart rate and slightly diminishes diastolic blood pressure in individuals with a lower possibility of having coronary artery disease (7); on the other hand, poststress left ventricular ejection fraction decreases significantly in patients with ischemia (3,8) because of end-systolic ventricular dilation (9,10) and inadequate ventricular contraction (11,12). We detected a decrease in systolic blood pressure, diastolic blood pressure, and left ventricular ejection fraction after dipyridamole administration unrelated to the existence of side effects or abnormalities in ECG and scintigraphy scans.

We observed an increment in heart rate and a decrement in systolic blood pressure after dipyridamole infusion. Homma et al. (5) and Ignaszewski et al. (13), in 2 separate studies, have also reported similar results with both nonexercise and symptom-limited exercise scintigraphy with dipyridamole.

TABLE 2

Hemodynamic Parameters Before and After Dipyridamole with Respect to Side Effects, ECG Findings, and Scan Findings

Parameter	Category	Heart rate		Systolic blood pressure		Diastolic blood pressure		Ejection fraction	
		Before	After	Before	After	Before	After	Before	After
Side effects	No	82 ± 12	82 ± 13	139 ± 20	132 ± 20	79 ± 8	76 ± 9	60 ± 11	58 ± 12
	Yes	82 ± 10	92 ± 10*	133 ± 23*	131 ± 23	79 ± 10	72 ± 10*	53 ± 14	50 ± 14
ECG findings	Normal	82 ± 12	88 ± 13	139 ± 21	132 ± 20	79 ± 8	75 ± 9	64 ± 8	63 ± 8
	Abnormal	82 ± 11	90 ± 12	137 ± 20	131 ± 20	79 ± 9	75 ± 10	47 ± 13	44 ± 13
Scan findings	Normal	77 ± 8	82 ± 8	138 ± 22	131 ± 21	79 ± 8	75 ± 9	66 ± 7	65 ± 7
	Abnormal	88 ± 13	96 ± 13	138 ± 20	133 ± 19	78 ± 9	75 ± 9	50 ± 13	49 ± 14

* $P < 0.05$.

Data are mean ± SD.

A retrospective investigation on 933 subjects has revealed that patients who exhibited some form of untoward reaction to dipyridamole were 10% more liable to show an abnormal perfusion examination outcome (14). Meyers et al. have also described headache as being the most prevalent adverse effect of dipyridamole in patients undergoing dual-isotope ^{201}Tl rest/ $^{99\text{m}}\text{Tc}$ -sestamibi stress imaging (15). Laarman et al. have shown that low-level exercise during dipyridamole infusion causes fewer noncardiac side effects, a similar incidence of angina, and a superior frequency of ST-segment changes, compared with dipyridamole alone (4). Our study did not contain a group without exercise; however, noncardiac side effects (13%) were less frequent and ECG abnormalities (32.3%) were more common than in similar studies without exercise.

In a study on 3,911 patients to evaluate the mortality and morbidity of dipyridamole-thallium imaging, Ranhosky et al. reported 2 deaths due to myocardial infarction and 2 additional nonfatal myocardial infarctions, 6 subjects with acute bronchospasm, and the following percentages of patients with additional side effects: chest pain (19.7%), headache (12.2%), dizziness (11.8%), and ST-T changes (7.5%) (16).

We also found a positive correlation between having abnormal ECG or scintigraphy findings and the likelihood of exhibiting dipyridamole side effects, especially chest discomfort, headache, and dyspnea. A similar correlation has also been stated by Villanueva et al. between ST-segment depression and chest pain or ECG results and redistribution defects (17).

Furthermore, our study revealed no significant difference between peripheral hemodynamic response and central coronary defects, confirming the previous finding of Zhu et al (18). This finding may indicate that defects revealed by dipyridamole are important even when there is no distortion of peripheral hemodynamic response. We have categorized patients only as having normal or abnormal ECG and scintigraphy outcomes, and we did not additionally study the correlation of side effects and hemodynamic parameters with different types of ECG or

imaging abnormalities—a topic that demands further investigation.

CONCLUSION

This study demonstrated a correlation between hemodynamic variables and side effects but not with imaging findings or ECG findings.

ACKNOWLEDGMENTS

This study was performed under the sponsorship of Golestan University of Medical Sciences (grant 393). Thanks are extended to the colleagues at our institutes for technical help and data acquisition.

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