Comparison of Myocardial Blood Flow During Dobutamine-Atropine Infusion With That After Dipyridamole Administration in Normal Men

Eiji Tadamura, MD, PhD,* Hideo Iida, PhD,† Keiichi Matsumoto, RT,* Marcelo Mamede, MD,* Shigeto Kubo, MD,* Hiroshi Toyoda, MD,* Toshiaki Shiozaki, MD,* Takahiro Mukai, PhD,* Yasuhiro Magata, PhD,* Junji Konishi, MD, PhD*

Kyoto and Suita, Japan

OBJECTIVES The present study was designed to compare the absolute myocardial blood flow (MBF) after intravenous dipyridamole infusion with that during dobutamine-atropine administration in normal healthy male volunteers.

BACKGROUND Both safety and usefulness of dobutamine-atropine stress in myocardial perfusion imaging have been reported. However, no information exists on whether the magnitude of hyperemia achieved with dipyridamole and dobutamine-atropine is comparable.

METHODS Myocardial blood flow was measured with positron emission tomography and 15O-labeled water in 20 healthy young men (23 ± 3 years) 1) at baseline, 2) after dipyridamole infusion (0.56 mg/kg over 4 min), and 3) during dobutamine (40 μg/kg/min) and atropine (0.25 to 1.0 mg) infusion.

RESULTS The MBF was significantly increased during dipyridamole infusion and during dobutamine-atropine stress compared with at rest (4.33 ± 1.23 and 5.89 ± 1.58 vs. 0.67 ± 0.16 ml/min/g, respectively, p < 0.0001). Moreover, dobutamine-atropine infusion produced greater MBF compared with dipyridamole (p = 0.0011), while coronary vascular resistance did not differ significantly after dipyridamole administration and during dobutamine-atropine infusion (17.6 ± 7.9 vs. 18.6 ± 5.6 mm Hg/[ml/min/g], respectively).

CONCLUSIONS Near maximal coronary vasodilatation caused by dipyridamole is attainable using dobutamine and atropine in young healthy volunteers. Dobutamine in conjunction with atropine is no less effective than dipyridamole in producing myocardial hyperemia. (J Am Coll Cardiol 2001;37: 130–6) © 2001 by the American College of Cardiology

Exercise stress in conjunction with radionuclide perfusion imaging is a well-established diagnostic approach for detecting coronary artery disease (CAD) (1,2). However, many patients are unable to physically perform an adequate exercise for various reasons such as peripheral vascular disease, pulmonary disease, orthopedic problem, old age and physical conditioning. Consequently, pharmacological coronary vasodilators including dipyridamole (3–5), adenosine (3,6,7), or positive inotropic agents such as dobutamine (8–13) and arbutamine (14) have emerged as effective alternatives. Exercise or dobutamine alone produces less increase in myocardial blood flow (MBF) than either dipyridamole or adenosine (8,12,15,16). As a result, dobutamine is considered less effective as a pharmacological stress agent for detecting coronary artery disease (17).

Atropine use in conjunction with dobutamine infusion has been extensively utilized in pharmacological stress for functional imaging (18–24). This approach has been introduced in myocardial perfusion imaging, and its usefulness and safety have been confirmed (25–28). However, no information exists on whether the magnitude of hyperemia achieved with dipyridamole and dobutamine-atropine is comparable. The purpose of the present study was to compare the absolute MBF (ml/min/g) after intravenous (IV) dipyridamole infusion and that during dobutamine-atropine administration using positron emission tomography (PET) and 15O-labeled water in normal healthy volunteers.

METHODS

Subjects. We studied 20 normal male volunteers with an average age of 23 ± 3 years (range 20 to 35 years). No patient had a history of diabetes or hypertension. None of the participants had a history of cardiovascular disease or smoking. Entrance criteria included normal heart rate, blood pressure (BP) and resting and stress electrocardiogram (ECG) and a low probability for CAD (29). The investigative nature and potential risks of the study were explained to all subjects. Each subject gave written informed consent approved by the Kyoto University Ethics Committee.

PET imaging. All PET studies were performed after an 8-h fast. In addition, all volunteers were carefully instructed to refrain from intake of caffeine-containing beverages or foods within 24 h before the study.

The study protocol is shown in Figure 1. On the first day, MBF was measured at rest and after dipyridamole infusion. Each subject was positioned in the gantry of the PET...
camera (Advance, General Electric Medical Systems, Milwaukee, Wisconsin) with the aid of ultrasound. The characteristics of this camera have been previously described (30). The spatial resolution of the reconstructed clinical PET images is \( \approx 8 \) mm in full-width half-maximum at the center of the field of view, and the axial resolution is \( \approx 4 \) mm (31). The subjects were lying supine in the PET scanner with their arms out of the field of view. Heart rate, BP and ECG were monitored continuously during the PET studies.

A 10-min transmission scan using two rotating \(^{68}\)Ge pin sources was made for the attenuation correction. After a transmission scan, subjects were requested to inhale \([^{15}\text{O}]\text{CO}\) for 2 min. After inhalation, carbon monoxide was allowed to combine with hemoglobin in red blood cells for 3 min before a 4-min static scan was started. During the scan period, three blood samples were drawn at 2-min intervals and radioactivity was measured. A 10-min period was allowed for \([^{15}\text{O}]\text{CO}\) radioactivity decay before the flow measurements. Flow was measured at rest and 3 min after the end of IV administration of dipyridamole (0.56 mg/kg body weight over 4 min). Approximately 740 MBq of \([^{15}\text{O}]\text{H}_2\text{O}\) was injected intravenously over 2 min and a 20-frame dynamic PET scan was performed for 6 min consisting of \(6 \times 5\)-s, \(6 \times 15\)-s and \(8 \times 30\)-s frames. All data were corrected for dead time, decay and photon attenuation.

Within a week, the same scan was repeated during infusion of the dobutamine and atropine. Two catheters were inserted: one for dobutamine infusion and another for blood sampling and infusion of atropine and \([^{15}\text{O}]\text{H}_2\text{O}\). Dobutamine infusion was started at a dose of 5 \(\mu\text{g/kg/min}\) followed by 10 \(\mu\text{g/kg/min}\) (3-min stages), increasing by 10 \(\mu\text{g/kg/min}\) every 3 min to a maximum of 40 \(\mu\text{g/kg/min}\). Atropine was administered in 0.25-mg splits at 1-min intervals to a maximal dose of 1.0 mg in subjects not achieving the target heart rate (85% of age-predicted maximal heart rate) (19). Subjects were asked to rate reactions or symptoms on a scale from 0 (no complaint) to 10 (intolerable). If the score reached 6, atropine was not given to the maximal dose even when the target heart rate was not achieved. After atropine was given, \([^{15}\text{O}]\text{H}_2\text{O}\) PET scan was initiated. Subsequently, \([^{15}\text{O}]\text{CO}\) and transmission scans were obtained as described above during infusion of 40 \(\mu\text{g/kg/min}\) of dobutamine.

**Data analysis.** The analysis of PET images was conducted with an image analysis package (Dr. View; Asahi-Kasei, Tokyo, Japan) and special dedicated software package (32). The PET images including transmission images, \([^{15}\text{O}]\text{CO}\) images, and \([^{15}\text{O}]\text{H}_2\text{O}\) dynamic images were reoriented into short-axis planes. Myocardial regions of interest

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**Figure 1.** Individual values of average myocardial blood flow (MBF) at rest, after dipyridamole infusion and during dobutamine-atropine infusion.
(ROIs) were drawn in the anterior, lateral, inferior and septal walls of a midventricular slice. Values of regional MBF (ml/min/g) were calculated according to the previously published method using a single-compartment model (33–35). This method has introduced a concept of the water-perfusable tissue fraction to solve the problem of the partial volume effect and cardiac wall motions. The water-perfusable tissue fraction is defined as the fractional mass of the tissue that is rapidly exchanging water within an ROI. Thus, this represents the recovery coefficient of the myocardial signal in the ROI. The water-perfusable tissue fraction is determined from the kinetic model analysis. Therefore, the method we have used to calculate MBF is theoretically free from the partial volume effect. The arterial input function was obtained from the left ventricular time-activity curve using a previously validated method in which corrections were made for the limited recovery of the left ventricular ROI and the spillover from the myocardial activities (36). In addition, a mean MBF value was obtained for each study by averaging the values of the four myocardial segments. To relate BP as an index of coronary driving pressure to the hyperemic blood flow, an index of coronary vascular resistance (CVR) (mm Hg/[ml/min/g]) was calculated by dividing the mean arterial pressure by blood flow (5,37).

**Statistical analysis.** Statistics were calculated with a commercially available personal computer software program (StatView-J 5.0, Abacus Concepts, Berkeley, California). Values are expressed as the mean ± SD. The regional MBF in four myocardial segments was compared by one-way analysis of variance (ANOVA). Repeated measures ANOVA was used to compare the groups with respect to changes in hemodynamic data, MBF and CVR. The statistical significance of intergroup differences was assessed using the Scheffe F test. A value of p < 0.05 was considered statistically significant.

**RESULTS**

**Hemodynamic responses.** Hemodynamic data at rest, after IV dipyridamole infusion and during IV administration of dobutamine and atropine are shown in Table 1. Diastolic and systolic BP increased during dobutamine-atropine infusion compared with at rest or after dipyridamole infusion (p < 0.0001). Heart rate increased significantly after dipyridamole infusion (p < 0.0001) and during dobutamine-atropine infusion (p < 0.0001). Heart rate during dobutamine-atropine infusion was still higher than during dipyridamole infusion (p < 0.0001). Rate-pressure product increased significantly after dipyridamole infusion (p = 0.0004) and during dobutamine-atropine infusion (p < 0.0001) compared with at rest (9324 ± 1864 and 24,609 ± 2898 vs. 6386 ± 1510 mm Hg · beats/min, respectively).

Side effects during dipyridamole infusion and during dobutamine-atropine administration. No serious side effects occurred during either of the two stress tests. In dobutamine-atropine stress, every subject received maximal dose of 40 μg/kg/min. No control subject reached target heart rate by dobutamine alone. Therefore, atropine was infused at least 0.25 mg in every subject. Mean dose of atropine was 0.45 ± 0.14 mg. Finally, 14 subjects (70%) reached the target heart rate, whereas two subjects failed to reach the target heart rate despite receiving the maximal dose of dobutamine and atropine. Atropine was not given to the maximal dose (1.0 mg) in four subjects without achieving the target heart rate, owing to palpitation and anxiety in one subject, headache and anxiety in another subject, and nausea in two subjects. Minor adverse reactions including shortness of breath, palpitation, headache, anxiety, nausea and dyspnea occurred in 14 subjects during dobutamine-atropine infusion, but in only 7 subjects after dipyridamole infusion (chi-square = 4.91, p < 0.05) (Table 1). The minor reactions of dobutamine-atropine infusion subsided after the study without treatment. Even when the reactions were not present, aminophylline (60 to 120 mg) was administered in every subject at the end of dipyridamole studies as part of our routine procedure. Minor reactions associated with dipyridamole administration promptly disappeared after aminophylline infusion.

**MBF at rest, after dipyridamole infusion and during dobutamine-atropine infusion.** The regional values of MBF measurements at rest, during dipyridamole infusion and during dobutamine-atropine infusion are shown in Table 2. No regional difference of MBF was noted at rest, during dipyridamole infusion or during dobutamine-atropine infusion.

Mean values of MBF and CVR at baseline, after IV dipyridamole and during dobutamine-atropine infusion are given for each subject in Table 1 and illustrated in Figures 1 and 2. The MBF at rest ranged from 0.52 to 1.00 ml/min/g (average 0.67 ± 0.16). During dipyridamole infusion, MBF ranged from 1.72 to 6.20 ml/min/g (average 4.33 ± 1.23). With IV infusion of dobutamine-atropine, MBF ranged from 2.86 to 9.51 ml/min/g (average 5.89 ± 1.58). Thus, mean MBF increased significantly with IV dipyridamole (p < 0.0001) and with dobutamine-atropine (p < 0.0001). Moreover, MBF during dobutamine-atropine infusion was greater than during dipyridamole infusion (p = 0.0011) (Fig. 1).

Mean CVR at rest, after dipyridamole infusion, and during dobutamine-atropine infusion was 116.4 ± 31.5, 17.6 ± 7.9 and 18.6 ± 5.6 mm Hg/(ml/min/g), respectively (Fig. 2). The CVR decreased significantly with dipyridamole (p < 0.0001) and with dobutamine-atropine (p < 0.0001) compared with at rest. However, CVR did not differ significantly after dipyridamole infusion and during dobutamine-atropine stress despite the significant difference in MBF.
Table 1. Hemodynamic Variables, Myocardial Blood Flow and Side Effects at Rest and During Pharmacological Stress in 20 Normal Men

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<th>BP (mm Hg)</th>
<th>MBF (ml/min/g)</th>
<th>Heart Rate (beats/min)</th>
<th>BP (mm Hg)</th>
<th>MBF (ml/min/g)</th>
<th>Heart Rate (beats/min)</th>
<th>BP (mm Hg)</th>
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<tr>
<td>23 ± 3</td>
<td>63 ± 10</td>
<td>101 ± 11/60 ± 8</td>
<td>0.67 ± 0.16</td>
<td>92 ± 10</td>
<td>100 ± 11/52 ± 13</td>
<td>4.33 ± 1.23</td>
<td>163 ± 14</td>
<td>151 ± 14/77 ± 13</td>
<td>5.89 ± 1.58</td>
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BP = blood pressure; MBF = myocardial blood flow.
DISCUSSION

The present data demonstrated that dobutamine-atropine stress produced greater increase in MBF than did dipyridamole stress, whereas CVR did not differ significantly during these pharmacological stress tests. These findings indicate that dobutamine-atropine stress induces near maximal vasodilatation and that the difference of MBF during these two pharmacological stress tests is caused by the difference of coronary driving pressure.

The effect of dipyridamole and dobutamine on MBF. Dipyridamole is a coronary artery vasodilator that increases the extracellular concentration of adenosine by blocking its cellular reuptake and metabolism (38). The standard dose of dipyridamole (0.56 mg/kg over 4 min) can induce maximum or near-maximal coronary vasodilatation in most subjects (3,39). On the other hand, the mechanism of action of dobutamine involves stimulation of beta-1, beta-2 and alpha-1 receptors, resulting in positive inotropic and chronotropic effects (16). It is believed that dobutamine increases myocardial oxygen demand, thereby increasing MBF (16). Thus, dobutamine alone produces less increase in MBF than either dipyridamole or adenosine (8).

Comparison with the previous studies. According to previous studies, MBF and CVR after dipyridamole infusion are 3.5 to ~5 ml/min/g and ~20 mm Hg/(ml/min/g) using PET and 15O-labeled water in healthy volunteers of similar age groups (4,5). The values of ~4 ml/min/g and ~18 mm Hg/(ml/min/g) obtained in the present study were in agreement with previous findings. By contrast, Krivokapich et al. (8) reported that the mean value of MBF during infusion of 40 μg/kg/min of dobutamine alone was 2.25 ml/min/g in healthy volunteers using PET and [13N] ammonia. To the best of our knowledge, this is the first study to provide quantitative values of MBF during high dose of dobutamine (40 μg/kg/min) and atropine infusion in normal healthy volunteers. Unexpectedly, infusion of dobutamine and atropine produced greater MBF than the standard dose of dipyridamole infusion. Moreover, the values of ~6 ml/min/g during infusion of dobutamine-atropine is far above the values reported by Krivokapich et al. (8). It is believed that this difference of MBF was partly caused by the increased heat rate associated with atropine infusion. The mean heart rate during the peak dobutamine infusion was 110 beats/min (8), whereas the value during the dobutamine-atropine stress in the current study was 163 beats/min. The difference of tracer for flow measurements may be partly responsible for this significant difference. The MBF estimated by [13N] ammonia tends to be lower than that by 15O-labeled water (10).

According to previous reports, dobutamine- or exercise-induced increases in MBF are proportional to cardiac work (10,12,15). In the current study, the average MBF increased 8.8-fold with dobutamine-atropine infusion, whereas rate-pressure product increased only four-fold. Thus, the change

<table>
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<th>Rest</th>
<th>Dipyridamole</th>
<th>Dobutamine-Atropine</th>
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<td>Anterior</td>
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<td>5.89 ± 1.68</td>
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<tr>
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<td>5.85 ± 1.57</td>
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<td>Septal</td>
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Figure 2. Individual values of average coronary vascular resistance (CVR) at rest, after dipyridamole infusion and during dobutamine-atropine infusion.
of MBF due to dobutamine-atropine was markedly greater than that of rate-pressure product, suggesting the presence of coronary vasodilatation effect when atropine and dobutamine were infused together. In fact, CVR during dobutamine-atropine infusion and after dipyridamole infusion did not differ significantly (Fig. 2). The difference of MBF during the two different myocardial stress tests is considered to be caused simply by the difference of coronary driving pressure. The physiological explanation for coronary vasodilatation effect of dobutamine-atropine infusion cannot be provided by the current study. The increase of MBF obtained by atropine may be caused by the increase of heart rate and consequently the myocardial oxygen demand. This sort of active hyperemia may be induced by accumulation of metabolites and certain vasoactive agents, particularly adenosine.

For this issue, further studies are needed.

Clinical implications of dobutamine-atropine stress. Minor reactions appeared more frequently in dobutamine-atropine stress than in dipyridamole stress. In terms of symptoms and reactions, dipyridamole may be recommended as a pharmacological stress agent. As is suggested elsewhere (16), patients who cannot exercise and who are not good candidates for dipyridamole or adenosine because of a history of chronic obstructive pulmonary disease, asthma or high-degree atrioventricular block will be good candidates for dobutamine-atropine stress. Other candidates include patients who took caffeine or used medications containing theophylline before a dipyridamole or adenosine myocardial perfusion imaging. In addition, one of the advantages of dobutamine over the vasodilator agents is the ability to assess the ischemic threshold with dobutamine. Moreover, the current study demonstrated that dobutamine in conjunction with atropine produced greater increase in MBF compared with dipyridamole. Thus, dobutamine-atropine has a potential to surpass dipyridamole or adenosine in producing flow disparity between myocardial regions supplied by normal and stenotic arteries. The present theory is in agreement with the findings by Levine et al. (40), who showed that the size of myocardial perfusion defects induced by dobutamine was larger than that induced by dipyridamole in patients with CAD.

Conclusions. High doses of dobutamine with atropine produced greater MBF than did the standard dose of dipyridamole and without a significant difference in CVR. These data suggest that near maximal coronary vasodilatation caused by dipyridamole is attainable using dobutamine and atropine in healthy young men. Dobutamine in combination with atropine is considered no less effective than dipyridamole for producing myocardial hyperemia.

Reprint requests and correspondence: Dr. Eiji Tadamura, Department of Nuclear Medicine and Diagnostic Imaging, Kyoto University Graduate School of Medicine, 54 Shogoinkawahara, Sakyo-ku, Kyoto, 606-8507, Japan. E-mail: et@kuhp.kyoto-u.ac.jp.

REFERENCES

20. Lee CY, Pellikka PA, McCully RB, Mahoney DW, Seward JB. Nonexercise stress transthoracic echocardiography: transesophageal