Adenosine Myocardial SPECT - Its Efficacy and Safety and Correlation with Coronary Angiogram

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Abstract

Objective: The aim of this study was to determine the safety and efficacy of adenosine Tc99m sestamibi myocardial perfusion study under controlled conditions and to correlate the adenosine Tc99m sestamibi perfusion defects and the coronary angiography in patients investigated for coronary artery disease.

Methods: This prospective study included 122 consecutive patients who underwent adenosine Tc99m sestamibi single photon emission computed tomography (SPECT) myocardial perfusion study. Seventy two patients had coronary angiographic correlation. All the patients who were referred by the cardiologists for stress myocardial perfusion scan who could not be stressed physiologically for one reason or the other were included in the study.

Results: Among the coronary angiography group the overall sensitivity, specificity, positive predictive value and negative predictive value of adenosine Tc99m sestamibi single photon emission computed tomography myocardial perfusion study for detecting significant coronary obstruction (diameter ≥ 50%) were 94.4%, 79%, 85% and 92% respectively. The side effects were transient and required no treatment.

Conclusion: We conclude adenosine Tc99m sestamibi single photon emission computed tomogram myocardial perfusion study is a reliable test with high sensitivity and specificity for the detection of coronary artery disease.

INTRODUCTION

Over the last two decades, many new methods have been developed for diagnosing and managing coronary artery disease. Pharmacological coronary vasodilatation as an adjunct to myocardial perfusion stress imaging has become increasingly popular in the evaluation of patients with coronary artery disease, in view of the large number of patients who cannot perform an adequate exercise test or in whom contraindications render exercise inappropriate. Myocardial perfusion scintigraphy provides very useful information in the evaluation of patients with coronary artery disease (CAD). It has been used in combination with exercise which has gained wide acceptance as an accurate technique for the detection and localisation of myocardial ischemia, functional significance of coronary artery stenoses and risk stratification of patients with CAD. However this technique cannot be used for those patients who cannot exercise due to a variety of musculoskeletal disorders, peripheral vascular disease, congestive heart failure, hypertension, neuromuscular ailments and also in patients with resting ST-T changes in whom the results of exercise tests may prove inconclusive. In addition, 25-30% of patients referred for myocardial perfusion imaging cannot achieve adequate workloads of exercise, which might significantly reduce the sensitivity for detecting CAD. In these patients vasodilation with intravenous adenosine infusion results in increase in myocardial blood flow, a physical response similar to that of physical exercise. Our study was aimed to establish the diagnostic efficacy of Adenosine Tc99m sestamibi myocardial perfusion SPECT study (AMPS) in correlation with coronary angiography (CAG).

Adenosine

Adenosine is a small heterocyclic molecule with a purine base and an attached sugar that is naturally found in tissues throughout the body and regulates blood flow in various vascular beds including the myocardium. Adenosine is produced intracellularly, but does not exert its effects until it leaves the intracellular environment and interacts with A1 and A2 receptors in the coronary arterioles. This results in an...
increase in adenylyl cyclase and decrease in calcium uptake, which leads to coronary vasodilatation thereby bringing a heterogeneity in coronary blood flow causing a coronary steal phenomenon and no true ischaemia.\textsuperscript{5,6} Theophylline and caffeine block the adenosine receptor interaction by their structural similarities with the single exception of methyl radical.\textsuperscript{7} Due to the rapid intracellular transport and metabolism of adenosine, its plasma half life is estimated to be less than 2 seconds, so this drug should be given as a continuous infusion.\textsuperscript{5,7} Adenosine induces coronary hyperemia in most patients at an intravenous dose of 140µg/min with a mean coronary blood flow of 4.4 ± 0.9 comparable to that of papaverine (4.8 ± 0.9).\textsuperscript{8} Cardiac effects of adenosine in addition to vasodilatation are transient bradycardia, decrease in systolic and diastolic blood pressures, increase in coronary blood flow 4-6 times the basal flow and decreased AV conduction.\textsuperscript{9} The extra-cardiac effects are stimulation of respiration, increase in cerebral blood flow, reduction in renal blood flow, abdominal cramps and warmth.\textsuperscript{9} The side effects reported were chest pain, headache, dizziness, flushing, dyspnnea, hypotension, nausea, ST-T changes in ECG and bronchospasm.\textsuperscript{10} The ability to produce maximal coronary vasodilation with shorter duration of action and limited side effects has made adenosine an agent of choice for pharmacological stress imaging.\textsuperscript{7,11}

**Material and Methods**

**Material**

In this prospective study 122 consecutive patients who were suspected to have CAD with or without history of previous myocardial infarction (MI), referred for stress imaging were included. All these patients were unable to perform exercise stress test due to various reasons like neurological deficits, musculoskeletal disorders, osteoarthritis, peripheral vascular disease with claudication, congestive heart failure, hypertension, extreme obesity and general debility. Patients with history of bronchial asthma, AV conduction problems, hypotension (systolic BP < 90 mmHg), bradycardia (HR < 60/min) and drug intake of xanthine derivatives were excluded from the study. It included both the sexes in the age group between 31-70 years who were unable to perform adequate stress test. They had 12 lead electrocardiogram, routine blood test and echocardiogram earlier to the AMPS.

**Methods**

**Adenosine Myocardial Perfusion Gated SPECT Study**

A two-day adenosine myocardial perfusion gated SPECT study protocol was followed. All medications, coffee and tea were discontinued 48 hours before the study. Baseline data were obtained before each study, which included heart rate, blood pressure and 12 lead electrocardiogram. Adenosine was infused intravenously at the rate of 140µg/kg/min for a period of 6 minutes.\textsuperscript{3} At the third minute of infusion 10-15 mCi of Tc99m sestamibi was administered intravenously. Heart rate and blood pressure were continuously monitored and the chest was auscultated at 3 minute intervals during the infusion. 10-15 mCi of Tc99m sestamibi was administered intravenously at rest for the resting myocardial perfusion gated SPECT study on the second day.

**Acquisition and Processing of Data**

Tc99m sestamibi gated spect study was done 45 minutes after the administration of Tc99m sestamibi for both the adenosine stress and rest studies. Acquisition used low energy all purpose collimator, 180 degree acquisition over 64 projections, 25 seconds per projection with patients in supine posture and a 15% window centered on the 140 KeV peak in a Siemens diacam gamma camera with SPECT facility interfaced with a dedicated state of the art computer. Preprocessing was done with a Butter worth filter of order 5 with a cutoff frequency of 0.33. A ramp filter was used to reconstruct the set of transaxial tomograms. Short axis, vertical and horizontal long axes tomograms of the left ventricle (LV) were automatically extracted from the reconstructed transaxial tomograms by performing reorientation to the long axis of the LV. No attenuation or scatter correction was used.\textsuperscript{12}

**Interpretation**

Adenosine and rest myocardial perfusion gated SPECT with Tc99m sestamibi studies were assessed by a conventional approach for quantification of regional Tc99m sestamibi uptake and reversibility using Cardiac Emory toolbox software system (Siemens). Hard copies obtained in transverse, sagittal and coronal sections, were interpreted by three well trained nuclear medicine physicians independently for the presence, absence or reversibility of defects. Those defects which had agreement of at least two physicians of the three were considered. Results were recorded region and arterial supply-wise.

Coronary angiograms is done in the conventional way, were interpreted by three experienced interventional cardiologists who had no knowledge about the imaging data. The number, location and percentage diameter narrowing of coronary arteries were recorded for each patients. More than 50% narrowing in the diameter as detected by QCA of a major coronary artery or its branches were considered as significant.\textsuperscript{13}

**Statistical Analysis**

Results were expressed as mean value ± standard deviation. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and correlation coefficient analysis of AMPS with CAGs were done vessel and vascular territory-wise.

**Results**

One hundred and twenty two consecutive patients were referred for AMPS. Of the 86 abnormal AMPS studies 72 (83%) underwent CAG. None of the 36 normal AMPS studies had CAG. Sixty four patients (89%) were detected to have significant lesions by both CAG and myocardial perfusion study. Eight patients (11%) had insignificant CAD while having a positive AMPS result. The observed results territory-wise of AMPS against CAG are tabulated in the Table 1.
sensitivity, specificity and the predictive values for the observed results are shown in Table 2. The observed values and their sensitivity and specificity vessel-wise are given in Table 3. The correlation coefficient for LAD, LCX and RCA are +0.000022603, +0.00008684 and +0.00008987 respectively.

**Hemodynamic Effects**

During the adenosine infusion there was an increase in the hear rate (86 ± 15 beats/min), systolic BP (124 ± 18 mm Hg) and diastolic BP (85 ± 12 mm Hg).

**Adverse Effects**

Adverse effects were seen in 88% of the patients (Table 4). Most of the side effects were mild and transient in nature. None developed high degree AV block during the infusion of adenosine, warranting termination of the infusion. No serious untoward effects were noted as a result of adenosine infusion.

**DISCUSSION**

The current study was undertaken to correlate the diagnostic value of adenosine myocardial perfusion gated SPECT using Tc99m sestamibi with that of CAG for its efficacy and safety. Adenosine myocardial perfusion study was reported to be comparable with that of exercise stress SPECT testing with no significant differences between their sensitivity and specificity in the evaluation of CAD by Coyne et al. and Gupta et al.16 Adenosine tomography is superior to exercise for detecting CAD in patients who could not perform adequate exercise. Nishimura et al reported a significant increase in the quantitated adenosine tomographic perfusion defect size in patients undergoing adenosine infusion in comparison with exercise stress particularly in those when the exercise in inadequate.17

The present study demonstrated that AMPS was accurate for the detection of CAD. The overall sensitivity, specificity, PPV, NPV of the nuclear test in detecting CAD with ≥ 50% diameter stenoses were 93%, 81%, 83% and 90% respectively. This sensitivity and specificity were more or less similar to the previous studies reported (87% and 89% by Verani et al18 and 93% and 78% by Amanullah et al19). The sensitivity and specificity vessel-wise distribution were 94% and 79% which were comparable with that of the results obtained arterial territory-wise. The frequency of ST segment depression during the adenosine infusion was low (7%), but was highly specific for reversible myocardial perfusion defects, which was also observed in a larger study group by Erik Marshal et al.20 Our observation that transient LV dilatation seen during the adenosine nuclear test is of low sensitivity, but it is highly specific for patients with multivessel critical stenoses needs further elaborate evaluation. The specificity might be more when used as a marker of sensitivity than marker of number of perfusion defects noted. The AMPS showed a positive correlation coefficient with that of coronary angiogram with values +0.000022603, +0.00008684, +0.00008987 respectively for LAD, LCX and RCA territories.

Two particularly attractive aspects of adenosine are its rapid onset of action and extremely short half-life.8,21 However the adverse effects reported were transient and needed no

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**Table 1 : Territory wise tabulation of AMPS vs coronary angiogram**

<table>
<thead>
<tr>
<th>Angiogram</th>
<th>LAD</th>
<th>Total</th>
<th>LCX</th>
<th>Total</th>
<th>RCA</th>
<th>Total</th>
<th>By each vessel</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPS + (Positive)</td>
<td>59</td>
<td>2</td>
<td>61</td>
<td>11</td>
<td>42</td>
<td>27</td>
<td>5</td>
<td>32</td>
</tr>
<tr>
<td>MPS - (Negative)</td>
<td>1</td>
<td>10</td>
<td>11</td>
<td>3</td>
<td>27</td>
<td>30</td>
<td>3</td>
<td>37</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>12</td>
<td>72</td>
<td>34</td>
<td>38</td>
<td>72</td>
<td>30</td>
<td>42</td>
</tr>
</tbody>
</table>

AMPS - Adenosine myocardial perfusion SPECT study; LAD - Left anterior descending artery; LCX - Left circumflex artery; RCA - Right coronary artery

**Table 2 : Sensitivity, specificity, PPV and NPV of the data from Table 1**

<table>
<thead>
<tr>
<th>By each vessel</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD</td>
<td>98%</td>
<td>83%</td>
<td>93%</td>
<td>89%</td>
</tr>
<tr>
<td>LCX</td>
<td>91%</td>
<td>71%</td>
<td>73%</td>
<td>90%</td>
</tr>
<tr>
<td>RCA</td>
<td>90%</td>
<td>88%</td>
<td>84%</td>
<td>92%</td>
</tr>
<tr>
<td>Total</td>
<td>94%</td>
<td>79%</td>
<td>85%</td>
<td>91%</td>
</tr>
</tbody>
</table>

**Table 3 : Total lesions detected in the vessels : AMPS vs CAG**

<table>
<thead>
<tr>
<th>By each vessel</th>
<th>Angio</th>
<th>Angio</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMPS +</td>
<td>117</td>
<td>20</td>
<td>137</td>
</tr>
<tr>
<td>AMPS -</td>
<td>7</td>
<td>72</td>
<td>79</td>
</tr>
<tr>
<td>Total</td>
<td>124</td>
<td>92</td>
<td>216</td>
</tr>
</tbody>
</table>

+Positive; -Negative; AMPS - Adenosine myocardial perfusion SPECT study; CAG - Coronary angiogram; Sensitivity - 94.4%; Specificity - 85%; PPV - 85%; NPV - 91%

**Table 4 : Adverse effects (all transient)**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>N=120</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest pain</td>
<td>54</td>
<td>45%</td>
</tr>
<tr>
<td>Throat pain</td>
<td>25</td>
<td>21%</td>
</tr>
<tr>
<td>Flushing</td>
<td>67</td>
<td>56%</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>21</td>
<td>18%</td>
</tr>
<tr>
<td>Headache</td>
<td>19</td>
<td>16%</td>
</tr>
<tr>
<td>GI discomfort</td>
<td>7</td>
<td>6%</td>
</tr>
<tr>
<td>Palpitations</td>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>Light headedness</td>
<td>3</td>
<td>2.5%</td>
</tr>
<tr>
<td>AV block</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

The present study demonstrated that AMPS was accurate for the detection of CAD.
treatment, though more studies have reported third degree AV block. From the imaging point of view, the myocardial uptake of Tc99m sestamibi with adenosine pharmacologic stress is higher than that of exercise stress thereby producing images of higher quality.

Pharmacologic myocardial perfusion imaging with adenosine has become an important and useful alternative to evaluate patients who cannot perform adequate exercise. Adenosine as a choice for pharmacological stress myocardial perfusion study is dependable in detecting CAD and also in the risk stratification of patients for future cardiac events. AMPS is accurate and reproducible. Antianginal drugs do not affect the pharmacological stress. So it is a convenient, safe and well tolerated non-invasive test with transient side effects.

REFERENCES