Pharmacologic and Exercise Stress Tests

Pharmacologic Stress Test: Adenosine

OVERVIEW

The purpose of this document is to specifically identify the critical components involved in performing a pharmacologic stress test with adenosine. This information serves as a standard for all nuclear cardiology laboratories. This document will cover **dosage and side effects, indications, contraindications, testing procedure, and indications for reversal of infusion.**

ADENOSINE

Adenosine induces direct coronary arteriolar vasodilation through specific activation of the A2A receptor. This results in a 3.5- to 4-fold increase in myocardial blood flow. Myocardial regions supplied by stenotic coronary arteries have an attenuated hyperemic response. Depending upon the severity of coronary stenosis and coronary flow reserve limitation, a relative flow heterogeneity is induced.

Adenosine generally does not cause myocardial ischemia. However, in a small percentage of patients with severe coronary artery disease (CAD), true ischemia may be induced because of a coronary steal phenomenon. Since the myocardial tracer uptake is proportional to the regional myocardial blood flow, a heterogeneous distribution of radiotracer occurs in the myocardium.

DOSAGE AND SIDE EFFECTS

Adenosine should be given as a continuous infusion of 140 mcg / kg / min. The package insert recommends a 6-minute protocol with the perfusion agent given at 3 minutes of infusion. Investigators have reported good results with infusion periods as short as 4 minutes (with the perfusion agent injected at 2 minutes).

Due to the short half-life of adenosine (<10 seconds), most side effects resolve in a few seconds after discontinuation of the adenosine infusion. However, the occasional patient may require administration of aminophylline for reversal of persistent symptoms.

Products should be inspected visually for particulate matter and discoloration prior to administration.

Side effects from nonselective activation of A1, A2B, and A3 receptors:

A1 Receptor	AV Block
A2B Receptor	Peripheral Vasodilation, Bronchospasm
A3 Receptor	Bronchospasm

Minor side effects occur in approximately 80% of patients:

Flushing	35% - 40%
Chest Pain*	25% - 30%
Dyspnea	20%
Dizziness	7%
Nausea	5%
Symptomatic Hypotension	5%

**Chest pain is nonspecific and is not necessarily indicative of the presence of CAD*

Other side effects include:

AV Block	7.6%
Second Degree AV Block	4%
Complete Heart Block	<1%
ST-Segment Depression of 1 mm or Greater	5% - 7%
Myocardial Infarction	Extremely rare

Adenosine results in a modest increase in heart rate and a modest decrease in both systolic and diastolic blood pressures.

INDICATIONS

Indications for an adenosine stress test are the same as for an exercise stress test (see Practice Points: Exercise Stress Test, p. 6) and are in the presence of the following conditions:

1) Inability to perform adequate exercise due to noncardiac physical limitations or lack of motivation.
2) Baseline electrocardiographic abnormalities such as left bundle branch block (LBBB), ventricular pre-excitation (Wolff-Parkinson-White syndrome), or permanent ventricular pacing.
3) Risk stratification of clinically stable patients after acute myocardial infarction (≥ 1 day) or following presentation to the emergency department with a presumptive acute coronary syndrome.

CONTRAINDICATIONS

Absolute contraindications for adenosine stress testing include:

1) Asthmatic patients with ongoing wheezing
   a. It has been reported that patients with adequately controlled asthma can undergo an adenosine stress test and can have pretreatment with 2 puffs of albuterol or a comparable inhaler. Bronchospasm is listed as an absolute contradindication in the package insert.
2) Second- or third-degree AV block without a pacemaker or sick sinus syndrome
3) Systolic blood pressure less than 90mm Hg
4) Recent use of dipyridamole or dipyridamole-containing medications
5) Methyl xanthenes such as aminophylline caffeine or theobromine block the effect of adenosine and should be held for at least 12 hours prior to the test.
   a. Pentoxifylline (Trental) does not appear to block the effects of adenosine.
6) Known hypersensitivity to adenosine
7) Unstable acute myocardial infarction or acute coronary syndrome

Relative contraindications for adenosine stress testing include:

1) Profound sinus bradycardia (heart rates < 40 beats/minute)

TESTING PROCEDURE

Patients should not eat 2 hours before the test. Patients may not consume caffeine-containing beverages or medications for at least 12 hours prior to testing.

This test requires an infusion pump and intravenous line with a dual-port Y-connector.

1) Adenosine infusion should be given at a rate of 140 mcg / kg / min.
   a. For patients deemed to be at a higher risk for complications (borderline hypotension, controlled asthma), adenosine infusion may be started at a lower dose (70 to 100 mcg / kg / min). The dose may then be increased to 140 mcg / kg / min as tolerated and the injection of the radiotracer given at the halfway point of the protocol.

2) Blood pressure should be monitored every minute during infusion and until stable in recovery (minimum of 3 minutes).
3) Obtain a 12-lead EKG every minute during the adenosine infusion and until stable in recovery (minimum of 3 minutes).
4) The patient should be monitored in recovery until symptoms have resolved and there is no evidence of ischemia.

Note: *Anti-ischemic cardiac medications can decrease the diagnostic accuracy of vasodilator stress testing.*

COMBINATION OF EXERCISE AND ADENOSINE

The combination of low-level upright treadmill exercise (1.7 mph, 0% grade) during the adenosine infusion has been found safe. The combination reduces the side effects of adenosine, attenuates the adenosine-induced drop in blood pressure, and improves image quality by decreasing high hepatic and gut radiotracer uptake.

Low-level exercise may be performed in combination with pharmacologic stress but is not recommended in patients with LBBB or for patients with pacemakers.

INDICATIONS FOR REVERSAL OF ADENOSINE INFUSION

The adenosine infusion should be stopped early under any of the following circumstances:

1) Severe hypotension (systolic blood pressure < 80mm Hg)
2) Development of symptomatic or persistent second-degree or complete heart block
3) Wheezing
4) Severe chest pain associated with ST depression of 2 mm or greater
5) Signs of poor perfusion (pallor, cyanosis, cold skin)
6) Technical problems with the monitoring equipment
7) Patient's request to stop

SUGGESTED READING

Bokhari S, Ficaro EP, McCallister BD. Adenosine stress protocols for myocardial perfusion imaging. J Nucl Cardiol 2007;14:415-6.

Henzlova MJ et al. ASNC Imaging Guidelines for Nuclear Cardiology Procedures: Stress protocols and tracers. J Nucl Cardiol 2009; doi: 10.1007/s12350-009-9061-5.

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