

Attenuating Severe or Persistent Adverse Events Associated With Vasodilatory Pharmacologic Stress

INTRODUCTION

As with any medication, vasodilatory pharmacologic stress agents carry a risk of causing adverse events (AEs) in patients after administration. There may be instances where the effects are severe or persistent enough to warrant pharmacologic intervention, based on clinical judgment and lab protocol. Understanding the mechanism of action of pharmacologic stress agents will help you to be better equipped to manage AEs in cardiac myocardial perfusion imaging (MPI) with pharmacologic stress.

ADVERSE EVENTS ASSOCIATED WITH PHARMACOLOGIC STRESS AGENTS

The most common AEs associated with pharmacologic stress agents include flushing, chest pain, dyspnea, dizziness, nausea, symptomatic hypotension, shortness of breath, and headache.¹ Pharmacologic stress agents have an incidence of AEs (for some, more than 50% of patients)¹ because the drugs induce or mimic a specific physiologic effect. The nuclear lab staff should be prepared to clinically manage them when necessary. This means that trained staff, resuscitative equipment, and a drug to counter the effects of vasodilatory pharmacologic stress should be available prior to drug administration. Serious adverse events that are most often associated with the administration of pharmacologic stress agents are listed in Table 1.² Reversal agents should always be available to attenuate severe and/or persistent side effects. In addition, patients should be made aware of effects they may experience prior to pharmacologic stress administration.

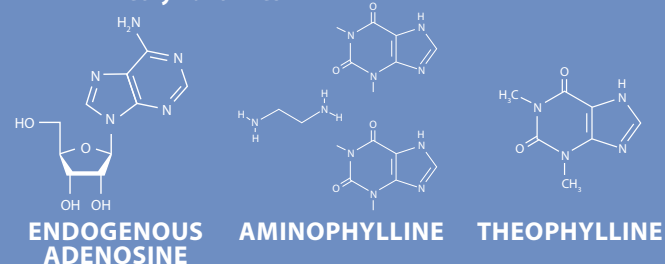
Table 1. Serious adverse events that may be associated with pharmacologic stress administration²

Anaphylaxis	Myocardial infarction
Angina	Myocardial ischemia
Bronchospasm	Respiratory arrest
Cardiac arrest	Seizure
Cardiac dysrhythmia	Sinoatrial block
Cerebrovascular accident	Syncope
Complete atrioventricular block	Ventricular arrhythmia
Hypertension	Ventricular fibrillation
Immune hypersensitivity reaction	Ventricular tachycardia
Liver failure	

VASODILATORY AGENTS FOR PHARMACOLOGIC STRESS

An agent used to counteract the effects of vasodilatory pharmacologic stress agents is aminophylline.¹ This drug is a methylated derivative of xanthine, or a methylxanthine. Methylxanthines are structurally similar to adenosine and are able to bind adenosine receptors, but not activate them (Figure 1).³ Instead, they act as antagonists of the adenosine receptors, inhibiting the natural actions of endogenous adenosine.⁴

Figure 1. Chemical Structure of Endogenous Adenosine and Methylxanthines



The physiologic effects of adenosine are mediated by 4 types of receptors located in various tissues throughout the body.⁵ The A_1 and A_2 adenosine receptors mediate the known cardiovascular effects of adenosine, and activation of the A_{2A} receptor stimulates coronary vasodilation.^{5,6} The vasodilatory pharmacologic stress agents either directly or indirectly activate the A_{2A} receptors in the coronary arteries to induce hyperemia.¹ By binding to and interfering with the activation of A_{2A} adenosine receptors in the coronary arteries, methylxanthines attenuate the effect of vasodilatory stress agents on coronary blood flow.

Aminophylline is a mixture of the methylxanthine theophylline and the compound ethylenediamine.⁷ It can be used clinically to reverse serious or persistent effects of vasodilatory pharmacologic stress agents. Historically, theophylline has been used as a reversal agent as well, but has not been extensively studied with all available pharmacologic stress agents.⁸ As with aminophylline, theophylline must be administered with caution and under the clinical judgment of healthcare professionals. Reference the individual package inserts for each pharmacologic stress agent for further information on dosing and administration of the

appropriate reversal agent to attenuate severe or persistent AEs. Methylxanthines may induce adverse events independent of those associated with pharmacologic stress, which must be addressed in accordance with product labeling and your particular pharmacologic stress testing protocols.

PATIENT PREPARATION FOR PHARMACOLOGIC STRESS TESTING

Patients should be instructed about what to expect with their cardiac MPI procedure. If the patient is a potential candidate for pharmacologic stress testing, nuclear lab staff should explain why he or she has been chosen for the test and how to prepare for it prior to the day of testing. This includes a discussion of foods, drugs, and beverages that contain methylxanthines (such as caffeine and theophylline) and the importance of abstaining from these products prior to a scheduled stress test, since they may interfere with the patient's imaging results.¹ It may be worthwhile to counsel patients who are scheduled for an exercise stress test to abstain from caffeine and other methylxanthine-containing products, in the event that they are unable to undergo the exercise test and are referred for pharmacologic stress testing.

For patients with known or suspected bronchoconstrictive disease, COPD, or asthma, their respiratory history and administration of pretest and posttest bronchodilator therapy should be discussed with their clinicians before scheduling an MPI procedure.⁹ As stated previously, patients should be informed about the effects of pharmacologic stress and the potential adverse events they may experience.

For additional information on patient preparation, visit **PharmStressTech.com** and read further *Tech Tips* related to this topic.

CONCLUSIONS

Preparation is vital to your everyday practice in the nuclear lab, including a course of action for any potential clinical scenario, including severe reactions to medications like a pharmacologic stress agent. Education and preparation may help to manage patient expectations associated with an MPI procedure.

Visit **PharmStressTech.com** for *Tech Tips* podcasts and interactive modules, which include an educational question-and-answer section.



References

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