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Case report

Late Aminophylline Reversal of Regadenoson Stress Testing in Patients with End Stage Renal Disease

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Abstract

Regadenoson is a widely used and well-tolerated vasodilator agent for pharmacologic stress myocardial perfusing imaging. In patients at higher risk of adverse reactions such as those with end stage renal disease, it can be reversed with early administration of aminophylline. However, little is known about late administration of aminophylline. This case report describes the efficacy of late aminophylline use in patients with end stage renal disease. Possible explanations for the prolonged pharmacodynamic effect of regadenoson in this group are discussed.

Keywords: Aminophylline, myocardial perfusion imaging, pharmacologic stress, regadenoson

Introduction

The selective A2A adenosine receptor agonist regadenoson is a widely used vasodilator for stress myocardial perfusion imaging.[1] In clinical practice, its use is attractive due to ease of administration, safety, tolerability, and fixed dosing.[2] Although it is reasonably well-tolerated in patients with end stage renal disease (ESRD), they have a higher incidence of adverse reactions including abdominal discomfort, diarrhea, and headache.[3] The gastrointestinal symptoms in particular may exhibit delayed onset.[3] Aminophylline, a nonselective phosphodiesterase inhibitor, can be administered to attenuate the side effect burden without compromising test sensitivity or specificity.[3,4]

In prior studies, aminophylline was administered between 2 and 15 min following regadenoson.[4,5] However, little is known about late (more than 30 min after regadenoson injection) use of aminophylline. In our experience, ESRD patients can have delayed or lingering symptoms responsive to late intravenous (IV) aminophylline. We present one such case and discuss potential mechanisms.

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Case Report

A 53-year-old black male with ESRD undergoing renal transplant evaluation was referred for a screening nuclear stress test. His medical history was otherwise notable for human immunodeficiency virus with a normal CD4 count and undetectable viral load on antiretroviral therapy. He was asymptomatic on arrival to the laboratory. Notable laboratory evaluation included the following (reference ranges shown parenthetically): Hemoglobin, 10.6 g/dL (13.5-17.5 g/dL); and creatinine 6.8 mg/dL (0.8-1.3 g/dL). Physical examination revealed an obese male with blood pressure (BP) of 158/100; pulse 75 beats/min, and saturation of 96% on room air.

He underwent pharmacologic nuclear stress testing per protocol. After 1.5 min of low-intensity ambulation he received IV regadenoson followed by technetium-99 injection. He reported transient shortness of breath and lightheadedness. There were no ischemic changes on the electrocardiogram. When he returned for stress imaging 45 min later he reported severe fatigue, nausea, and headache. An IV was restarted and 125 mg of IV aminophylline was administered. Symptoms quickly resolved, and stress images were acquired without issue. Perfusion imaging revealed no evidence of myocardial infarction or ischemia.

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Discussion

Regadenoson undergoes three pharmacokinetic phases characterized by half-lives of 2-4, 30, and 120 min, respectively. Pharmacodynamic effects of regadenoson cease after the second pharmacokinetic phase.[2] Similarly, adverse reactions typically resolve within 15 min with the exception of headache which resolves in most patients within 30 min.[2] Although regadenoson has an increased elimination half-life in renal impairment, the maximum observed plasma concentrations are not significantly altered.[6] Thus, there is no adjustment of the standard 0.4 mg regadenoson dose for renal function.[7] Although the magnitude of hemodynamic effects is similar in patients with normal versus impaired renal function,[8] the duration appears to differ. The decrease in diastolic BP[3] and increase in heart rate persist longer in patients with ESRD with the latter lasting up to 150 min.[7] This suggests a more prolonged pharmacodynamic phase with attendant side effects.

As in this case, we have observed a highly effective response to late administration of aminophylline for reversal of symptoms in patients with ESRD. Many of these patients are asymptomatic at the immediate conclusion of stress testing but develop symptoms in delayed fashion.[3] Placebo effect and coincidental resolution are not felt to be adequate explanations given the dramatic nature and reproducibility of this finding.

We, like others,[1,3] have a significantly higher rate of aminophylline reversal in patients with ESRD. To date little has been known about efficacy of aminophylline late (>30 min) after regadenoson injection. Standardized administration of aminophylline to patients with severe chronic kidney disease has been shown to be effective.[4] This represents one approach to the higher side-effect burden in this group of patients. Alternatively, it appears that, if necessary, patients with ESRD can also be reversed with aminophylline effectively at a late juncture.

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