Adenosine-induced severe acute respiratory distress in chronic obstructive pulmonary disease: a myth?

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Introduction

Adenosine is a widely used agent for pharmacologic stress testing during myocardial perfusion imaging (MPI). Adenosine induces an up to 4-fold increase in coronary blood flow and thus unmasks coronary stenosis [1]. Adenosine induces side effects in 50–80% of patients, which in general are mild and reverse within minutes after termination of drug administration [3]. Contraindications to adenosine include hypersensitivity to the substance, pronounced hypotension, symptomatic aortic stenosis, hypertrophic cardiomyopathy, higher degree atrioventricular block [4], asthma [5] or "bronchospasm" [6] and "severe bronchospasm" [4]. Many patients report shortness of breath during adenosine infusion, which has been shown not to be associated with any appreciable bronchospasm in patients with nor without chronic obstructive pulmonary disease (COPD) [5]. Accordingly, well-controlled COPD is not a contraindication to adenosine testing, and due to the very short half-life of the drug (<10 seconds) the risk of a significant bronchospasm is very low [5]. However, in one study, MPI with dipyridamole, a substance inhibiting cellular adenosine uptake and thereby raising extracellular adenosine concentrations, has been shown to induce significant and symptomatic bronchospasm in nearly 50% of patients with severe COPD scheduled for lung volume reduction surgery [7]. We herein report on the very rare case of severe acute respiratory distress induced by adenosine in a patient with moderate COPD.

Case report

A 78-years-old lady with a history of long-standing previous cigarette smoking (100 pack-years, stopped six years ago), coronary artery disease and recurrent chest pain was referred for MPI. She had known COPD with documented moderate non-reversible obstructive ventilatory defect, and was on regular treatment with inhaled steroids and long-acting beta-2-mimetics. Due to the presence of left-bundle branch block, adenosine MPI was performed. Of note, two previous MPIs (one with dipyridamole, and one with adenosine) had been uneventful. Before starting the adenosine infusion (140 µg/kg body weight/min) the patient denied shortness of breath, and pulmonary auscultation was normal. After the first minute of adenosine infusion the patient reported slight breathing problems, the clinical examination being normal at that time. When the patient reported progressive dyspnoea one minute later, there was moderate wheezing over all lung fields. The tracer (^{99m}Tc sestamibi) was immediately injected, and adenosine was stopped 20 seconds later, as the patient suddenly was unable to speak, had a markedly prolonged expirium, used the auxiliary respiratory muscles, and had massive wheezing over all lung fields. Repeated application of salbutamol by dose inhaler (four doses, one dose corresponding to 100 µg according to the manufacturer) did not improve dyspnoea, respiratory rate, and the intensity of wheezing. Finally, theophylline 50 mg IV was applied, resulting in an improvement of dyspnoea from "severe" to "less severe", a decrease in respiratory rate, and a marked reduction of the wheezing intensity within one minute, but complete normalisation occurred only after 20 minutes and inhalation with salbutamol/itrapropium.

Comment

This case highlights that i) adenosine can induce severe acute respiratory distress also in patients with COPD and fixed obstruction even though it is observed in only very rare cases, ii) the respiratory distress can be prolonged despite the very short half-life of adenosine, and iii) a direct antagonist of adenosine may be necessary to treat these patients. We did not document a reduction in the forced expiratory volume during the first second or peak expiratory flow. Therefore, we cannot assure that bronchospasm really occurred. However, the clinical picture and the response to theophylline were very suggestive of acute bronchospasm. However, medical history and spirometry test results did not indicate an asthmatic component.

Of note, we do not want to discourage adenosine use, as long as patients are informed about the frequent but mild and transient side effects. Adenosine is very suitable and efficient for practical use and is generally well tolerated. In our institution, only the described patient had remarkable problems, which is consistent with 0.4% of patients who undergo adenosine stress testing each year. In the first six months of the year 2006, 42% of 772 MPIs were performed using adenosine (either combined with low level exercise or as isolated pharmacologic stress test in patients with left-bundle-branch block, pacemaker rhythm, or those unable to do any physical exercise). However, as adenosine stress testing is further expanding (eg for perfusion magnetic resonance imaging, where the communication to the patient is more difficult), we want to point out that i) clinical judgment of the patients before and during adenosine studies is critically important, ii) the supervising physicians must be familiar not only with ECG changes associated with adenosine administration (ie atrioventricular block), but also with the herein reported type of complication, and iii) the presence of emergency drugs including theophylline or aminophylline is mandatory in all cases.

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