International Journal of Medicine and Medical Sciences ISSN: 2167-0404 Vol. 2 (10), pp. 209-210, October, 2012.
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Short Communication

Acute disabling epigastric pain during intravenous administration of amiodarone

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Received 06 August, 2012; Accepted 17 October, 2012

Amiodarone is a Class III antiarrhythmic agent used for cardioversion and prevention of recurrences of atrial fibrillation. However, its use is limited due to its side-effects resulting from the drug's long-term administration. The only acute and benign adverse reaction of intravenous amiodarone that has been reported is acute low back pain. We describe a patient who suffered an acute disabling epigastric pain, following treatment with intravenous amiodarone for atrial fibrillation. When treatment with amiodarone was abruptly interrupted, the epigastric pain was completely resolved. To our knowledge, there are no cases describing severe epigastric pain as an acute reaction to intravenous amiodarone administration. Intravenous, and rarely oral, administration of amiodarone has been related to a series of minor and major adverse reactions, indicating other constituents of the intravenous solution as the possible cause, possibly polysorbate 80. A possible correlation between acute epigastric pain and intravenous amiodarone loading is unproven; however it is of crucial importance for clinicians to be aware of this phenomenon, and especially since an acute epigastric pain is implicated in the differential diagnosis of cardiac ischemia.

Key words: Acute epigastric pain, intravenous amiodarone, antiarrhythmic.

INTRODUCTION

The use of medications has been inevitably linked to the risk of development of adverse reactions. It is estimated that adverse drug reactions may rank from fourth-to-sixth-leading cause of death in both hospitalized individuals and outpatients, thus representing a significant clinical issue (Lazarou et al., 1998). Amiodarone is a long established Class III antiarrhythmic agent recommended for cardioversion and prevention of recurrences of atrial fibrillation. We present a case of a woman who suffered a disabling epigastric pain following the intravenous administration of amiodarone.

CASE PRESENTATION

An 84-year old female presented to the emergency department of our hospital with a history consistent with retrosternal tightness and palpitations for the last 12 hours. The patient's personal history included a well-controlled arterial hypertension under irbesartan and hydrochlorothiazide. At the emergency department the patient was hemodynamically stable with a blood pressure of 150/80 mmHg, oxygen saturation 97%, respiratory rate 16 breaths/minute and normal body temperature. Heart auscultation revealed tachyarrhythmia and a mild systolic murmur. A 12-lead electrocardiogram (ECG) revealed atrial fibrillation with a rapid ventricular response of about 130 beats/min. The case of an acute coronary syndrome was excluded since a complete set of cardiac biomarkers were normal. The laboratory tests were within normal limits. Chest x-ray demonstrated a normal cardiothoracic index and no evidence of pulmonary congestion. A transthoracic echocardiogram showed minor mitral regurgitation. In view of the patient's clinical history, and the recent-onset atrial fibrillation, pharmaceutical cardioversion was decided and intravenous administration of amiodarone was initiated (loading dose of 5 mg/kg over 30 min). However, about 3 min after treatment initiation the patient complained of acute disabling epigastric pain. The patient denied any history of gastrointestinal symptoms. A few minutes later, hemodynamic deterioration appeared with hypotension and dyspnea. The ECG showed slow atrial fibrillation of about 50 beats/min with no evidence of heart block or

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ischemic changes. Treatment with amiodarone was abruptly interrupted and the epigastric pain was completely resolved within 10 min. Hemodynamic stability was reestablished with the administration of intravenous normal saline solution. The patient was admitted to the hospital for further monitoring and investigation. A second set of cardiac biomarkers were also normal. Atenolol for heart rate control, as well as low molecular weight heparin were initiated. Computed tomography of the abdomen showed no lesions of the alimentary organs that could be associated with the aforementioned epigastric pain. The patient was administered peros amiodarone, and on the third day of hospitalization the atrial fibrillation resolved to sinus rhythm. The patient was discharged with explicit instructions and medication.

DISCUSSION

Amiodarone comprises an effective antiarrhythmic agent for cardioversion of recent onset atrial fibrillation and maintenance of sinus rhythm (Fuster et al., 2011). However, there are significant limitations in its use due to its numerous side-effects resulting from the drug's long-term administration. Due to its notable lipophilicity and associated long half-life, the drug is accumulated in many different kinds of tissues and organs including the lung, the thyroid gland, the liver, the central nervous system and the cornea. Furthermore, cardiovascular side effects, such as bradycardia, heart block and hypotension have been clearly described in Stelfox et al. (2004) and Siddoway (2003).

Concerning the acute side effects of amiodarone, excluding cardiac ones that require immediate action, only one has been reported, that is acute low back pain. There are three cases reported concerning low back pain as a benign reaction to intravenous administration of amiodarone that are spontaneously resolved after cessation of the infusion (Korantzopoulos et al., 2005; Manzano-Fernández et al., 2010; Tsikrikas et al., 2010). To the best of our knowledge, there are no cases in the current literature describing disabling epigastric pain as an acute reaction to intravenous amiodarone administration.

Notably, intravenous, and rarely oral, administration of amiodarone has been related to a series of adverse reactions, indicating other constituents of the intravenous solution as the possible causative agent.

There are a number of reports suggesting that polysorbate 80 (polyoxenethylated sorbitan ester) – an excipient used to stabilize aqueous formulations of medications for parenteral administration, like amiodarone infusion – could be implicated in a variety of minor or major adverse reactions, the latter ranging from immunological and nonimmunological anaphylactoid reactions to direct tissue toxicity (Rhodes et al., 1993; Montagnani et al., 2011; Coors et al., 2005; Weiszhár et al., 2012).

Any possible correlation between acute epigastric pain and intravenous amiodarone loading remains to be clarified. We are fully aware of the fact that the described symptom could be either incidental or an early manifestation of the following hemodynamic instability. A possible mechanism for the epigastric pain appearance could be that polysorbate 80 caused the hypotensive response that resulted in transient secondary mesenteric ischemia. Several studies, concerning investigation of drug formulation vehicles in general toxicology, have demonstrated that intravenous administration of polysorbate 80 in canine species has been associated with an idiosyncratic reaction characterized by a prolonged depressor response. The resulting hypotension was caused by a marked release of histamine. Importantly, hypersensitivity (as assessed by clinical signs, ECG, and clinical pathology) was not observed in any species at the same dose level following oral administration of polysorbate 80 (Thackaberry et al., 2010).

According to adverse drug reaction probability scale proposed by Naranjo et al. (1981), the described symptom is designated as a possible reaction to amiodarone. However, until further similar reports come to light, we believe that it is of crucial importance for clinicians to be aware of this phenomenon, especially since an acute epigastric pain is implicated in the differential diagnosis of cardiac ischemia.

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