

## Atropine-Resistant Atrioventricular Block in Non-Q-Wave Myocardial Infarction: The Role of Low Dose Aminophylline (case report)

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### ABSTRAK

Selain Bezold-Jarisch reflex, perangsangan reseptor adenosin oleh adenosin yang dibebaskan dari jaringan miokard yang iskemi merupakan mekanisme kedua yang bertanggung jawab atas terjadinya blok atrioventrikuler (AV) pada inferior miokard infark akut. Aminofilin sebagai antagonis reseptor adenosin yang kompetitif, telah memperlihatkan efek dalam mengembalikan blok AV yang atropine-resistant akibat adenosin. Pada artikel ini, telah dilaporkan bahwa aminofilin dalam dosis 120 mg dapat mengembalikan blok AV yang atropine-resistant pada seorang pasien yang menderita non-Q-wave miokard infark akut yang kecil tanpa menimbulkan efek samping. Laporan ini menyarankan penggunaan dosis kecil aminofilin pada blok AV yang atropine-resistant yang muncul selama miokard infark akut.

### ABSTRACT

Besides Bezold-Jarisch reflex, activation of adenosine receptors by adenosine released from ischemic myocardial tissue is the second mechanism responsible for atrioventricular (AV) block during acute inferior myocardial infarction (MCI). Aminophylline, a competitive adenosine receptor antagonist has been shown to reverse this type of atropine-resistant AV block. In this article, an episode of atropine-resistant AV block was reversed by 120 mg of aminophylline, a competitive adenosine receptor antagonist, in a patient with a small non-Q-wave MCI, and without any adverse effect. This report suggests a use of low dose aminophylline in atropine-resistant AV block during acute MCI.

**Keywords:** Aminophylline, Atropine-resistant AV block.

### INTRODUCTION

It is well documented that atrioventricular (AV) block occurs more commonly in patients with inferior than anterior myocardial infarction (MCI).

According to Berger and Ryan review,<sup>1</sup> high-degree AV block complicating acute inferior myocardial infarction may be caused by Bezold-Jarisch reflex which is atropine-sensitive and occurs usually within 24 hours after the infarction, and activation of adenosine receptors by adenosine released from ischemic myocardium which is atropine-resistant, but may be aminophylline-sensitive. It occurs usually after 24 hours of infarction and is associated with a large infarct area.<sup>2</sup>

In this article, we report an atropine-resistant but aminophylline-sensitive of complete heart block, which occurs within 24 hours in a small non-Q-wave myocardial infarction.

### CASE REPORT

A 60-year-old woman was referred from the Air-force Hospital after being given Dopamine drip, Pethidine 50 mg, Cedocard 10 mg, and Nitrodisc who was diagnosed with acute non-Q-wave myocardial infarction complicated by severe hypotension and bradycardia.

She had an angina attack at 9.00 AM, and had been given anti-anginal therapy. However, at night she suffered from a typical infarction chest pain and drowsiness, which drove her to the hospital.

The risk factors from having coronary artery disease were diabetes mellitus and hypertension.

#### Physical examination on arrival

She looked pale and somnolence. Blood pressure (BP)=66/40 mmHg, heart rate (HR)=40 x/min, respiratory rate (RR)=24 x/min, normal jugular venous

pressure, weak heart sound, normal respiratory sound, and cold extremities.

ECG showed a second degree (Mobitz type II) AV-block, atrial rate: 96 x/min, ventricular rate: 44 x/min, normal QRS axis, ST- depression and T-inverted on lead I, aVL, V3-V6.

Laboratory findings: Hemoglobin: 8.7 g/l; Leukocytes: 8700/ $\mu$ l; Hematocrite: 27 vol%; Creatine kinase (CK): 242  $\mu$ l; Creatine kinase myocardial band (CKMB): 11.8  $\mu$ l; others were within normal limit.

**Management**

The patient was first given oxygen and atropine sulphate 0.5 mg (I.V). Soon after this her blood pressure rose to 120/70 mmHg. The ECG showed a sinus

tachycardia with ventricular rate of 110 x/min (Figure 1), and the patient resumed consciousness. However, after 10 minutes, the blood pressure dropped again accompanied with severe bradycardia. These events occurred repeatedly three times in a row.

While the temporary pace-maker was being prepared, she was given aminophylline 120 mg (2 mg/kgbw) followed by 0.2 mg/kgbw/hr drip. At this time, her blood pressure and heart rate could be restored to normal and stabilized, and her general condition improved.

She was then given medication for the non-Q-wave myocardial infarction and packed red cells for the anemia.

On the 4th day, the patient left the coronary care unit without any complication.

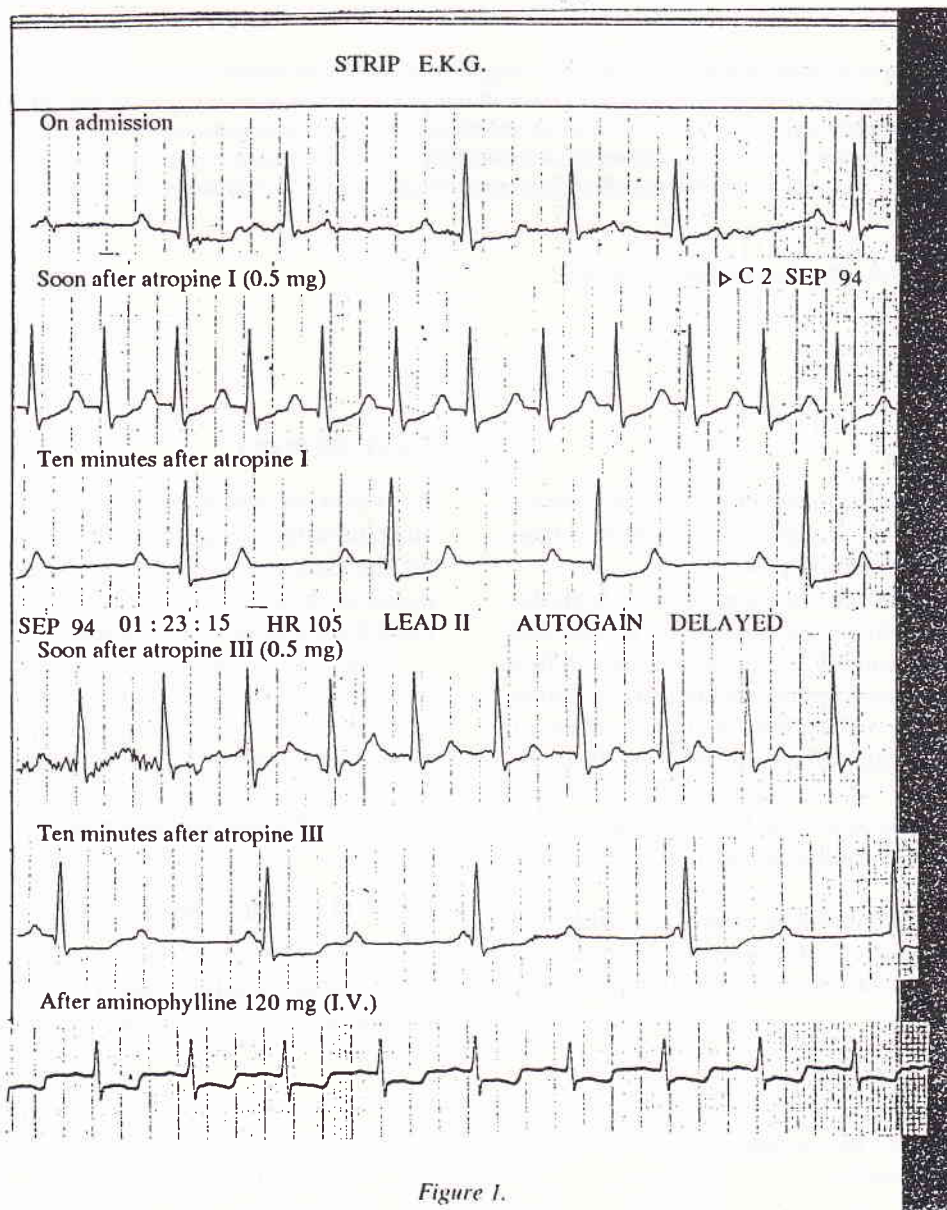


Figure 1.

## DISCUSSION

In the majority of cases, second or third degree heart block complicating inferior MCI are response to atropine.<sup>3</sup> However, heart block occurred after the first 24 hours in a large inferior MCI is usually atropine-resistant; because it is related to the release of adenosine by the ischemic myocardium, which stimulates a specific adenosine receptors and in turn depresses AV conduction.<sup>4</sup>

Aminophylline which possesses positive inotropic and chronotropic effects by blocking off adenosine receptor,<sup>4</sup> increasing adrenaline and noradrenaline release,<sup>5</sup> inhibiting cyclic nucleotide phosphodiesterase,<sup>6</sup> and increasing calcium entry<sup>7</sup> in the myocardial cells. It was therefore able to reverse the atropine-resistant complete AV block in acute inferior MCI,<sup>2,8</sup> and has been reported success in treating paroxysmal sinus bradycardia,<sup>9</sup> sick sinus syndrome,<sup>10</sup> and atrial fibrillation with a slow ventricular response.<sup>11</sup>

The conventional dose of aminophylline used to reverse atropine-resistant heart block<sup>2,8</sup> was 300-400 mg (5 mg/kgbw, given intravenously as a single dose). This was to maintain the blood level of aminophylline in the range of 10 - 15 mg/liter, as has been shown that in this therapeutic dose, aminophylline shortened sinoatrial conduction time, sinus node recovery time, and AV nodal functional refractory period.<sup>9</sup> However, it has also been shown that the serum concentration of aminophylline as low as 3.7 mg/liter improved sinus nodal function in patients with sinus bradycardia, which is related to antagonism of adenosine receptors.<sup>12</sup> Indeed, as in present report, low dose of aminophylline, that is 120 mg (2 mg/kgbw) could control the atropine-resistant complete heart block. Other than this, we have the same experience in two other cases where 120 mg of aminophylline could reverse atropine-resistant AV block complicating inferior MCI.

Complete AV block in acute MCI should be temporarily paced as recommended by American College of Cardiology/American Heart Association guidelines for the early management of patients with acute MCI, especially if there are symptoms of low cardiac output and atropine-resistant. However, temporary cardiac pacemaker may have many complications include ventricular arrhythmias, ventricular perforation, bleeding, infections, pneumothorax etc. More over, some hospitals may not have this facility. Therefore, looking for an alternative non-invasive pharmacological treatments for treating atropine-resistant AV block are needed.

Aminophylline has long been proven to be able to treat bradyarrhythmias associated with ischemic heart

disease.<sup>13</sup> The arrhythmogenic and vasodilatation effects of this agent have limited its use in this condition. However, these effects was found to occur mostly in the therapeutic serum concentrations ranged from 10-15 mg/l.<sup>9</sup> or more.<sup>14</sup> In low concentration, on the other hand, aminophylline induced pulmonary and systemic vasoconstriction<sup>15</sup> and was without adrenergic effect.<sup>10</sup>

In view of the fact that increased sympathetic activity generates triggered activity on myocardial cells,<sup>16</sup> theoretically, low concentration of aminophylline may not have arrhythmogenic effect.

The present data, in conjunction with previous experimental observations and case reports, support the other alternative use of low dose aminophylline in atropine resistant complete heart block complicating myocardial infarction.

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