



FROM FAILURE TO RESQUE: AMINOPHYLLINE IN ATROPINE-RESISTANT BRADYCARDIA – A CASE REPORT

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ABSTRACT

Background : Bradycardia with a heart rate below 50 bpm and hypoperfusion, is an emergency condition that requires prompt management. According to ACLS guidelines, atropine sulfate is the first-line medication. This case highlights the role of aminophylline as an alternative therapy in atropine-resistant bradycardia prior to the use of dopamine or epinephrine.

Case Illustration : A 73-year-old woman came to the emergency room with weakness and dyspnea. Physical examination revealed signs of pulmonary edema and hemodynamic instability. An ECG revealed sinus bradycardia with a rate of 24 beats per minute. Laboratory findings suggested an acute exacerbation of chronic kidney disease with hyperkalemia (5.56 mmol/L). The patient was immediately given atropine up to a maximum cumulative dose of

12 ampoules (3 mg), but showed no chronotropic response. Intravenous aminophylline 240 mg was then administered. Following aminophylline administration, the heart rate increased significantly to 82 beats per minute, followed by hemodynamic improvement and gradual resolution of pulmonary edema symptoms.

Discussion: The failure of atropine suggests that the bradycardia is likely mediated by purinergic pathways, rather than simply vagal overactivity. In renal failure and hyperkalemia, cellular metabolic stress leads to increased interstitial adenosine levels, which depress the sinoatrial and atrioventricular nodes via the A1 receptor. Aminophylline acts as a competitive antagonist at this receptor, thus restoring heart rate when parasympatholytic agents fail. Furthermore, aminophylline's potential to increase renal blood flow and its mild positive inotropic effect provide additional benefits in managing fluid overload and pulmonary edema.

Conclusion : Aminophylline can be considered as another treatment option for atropine-resistant bradycardia prior to the use of dopamine or epinephrine

Keywords: Bradycardia, Aminophylline, Atropine-resistant

INTRODUCTION

Bradycardia is generally defined as a heart rate below 60 beats per minute. It may occur as a normal physiological finding, particularly during sleep or in physically trained individuals, but it can also result from abnormalities in cardiac impulse generation or conduction. Pathological bradycardia may reduce cardiac output and compromise systemic perfusion. Clinically significant bradycardia may present with hypotension, altered mental status, ischemic chest discomfort, acute heart failure, or shock.¹

Management of bradycardia depends primarily on the presence of symptoms and cardiopulmonary compromise rather than on the heart rate alone. Initial management includes assessment of the airway, breathing, and circulation, together with identification and treatment of reversible causes. Atropine is recommended as the initial pharmacological treatment for symptomatic bradycardia with cardiopulmonary compromise.¹ However, the response to atropine may be inadequate in some patients. When bradycardia persists despite atropine, transcutaneous pacing and/or dopamine or epinephrine infusion may be considered, while transvenous pacing may be required in selected patients.¹

Aminophylline is a methylxanthine derivative with adenosine receptor antagonist activity. Its use has been reported in patients with symptomatic bradycardia, particularly when conventional treatment is ineffective or contraindicated.³ Adenosine plays an important role in cardiac electrophysiology. Activation of adenosine A1 receptors decreases sinoatrial node activity and slows atrioventricular conduction, producing negative chronotropic and dromotropic effects.² By antagonizing the effects of adenosine, aminophylline may increase sinoatrial node activity and improve atrioventricular conduction, thereby increasing heart rate.^{2,3} Although aminophylline is not part of the first-line treatment algorithm for adult bradycardia, previous reports have described its use in symptomatic bradycardia that is refractory to standard therapy.^{1,3} Evidence regarding its use in atropine-resistant bradycardia remains limited.

In this case report, we describe the use of aminophylline in a patient with atropine-resistant bradycardia. This case highlights the potential role of aminophylline as an alternative pharmacological treatment when the response to atropine is inadequate

CASE REPORT

A 73-year-old woman came to emergency room with weakness and dyspnea since 6 hours earlier. Physical examination revealed signs of pulmonary edema and hemodynamic instability. Blood pressure 80/60 mmHg with an ECG revealed sinus bradycardia with a rate of 24 beats per minute (figure 1). On the chest x-ray, pulmonary edema was found (figure 2). Laboratory findings suggested an acute exacerbation of chronic kidney disease (ACKD) with hyperkalemia (5.56 mmol/L). From these conditions, the patient was diagnosed with cardiogenic shock ec bradycardia extreme, ACKD with hyperkalemia and pulmonary edema.

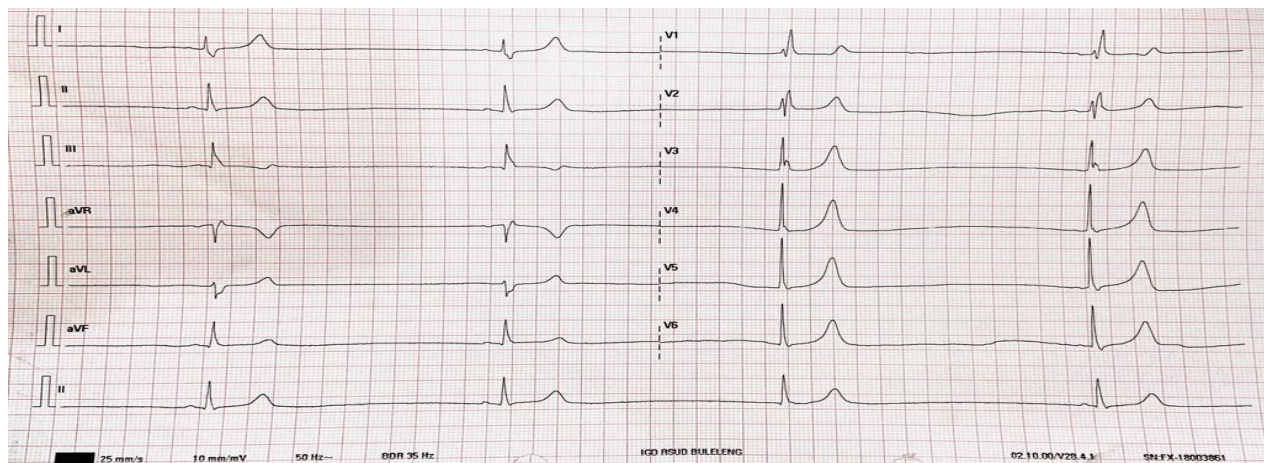


Figure 1. The ECG (before aminophylline administration) showed sinus bradycardia 24 beats/min

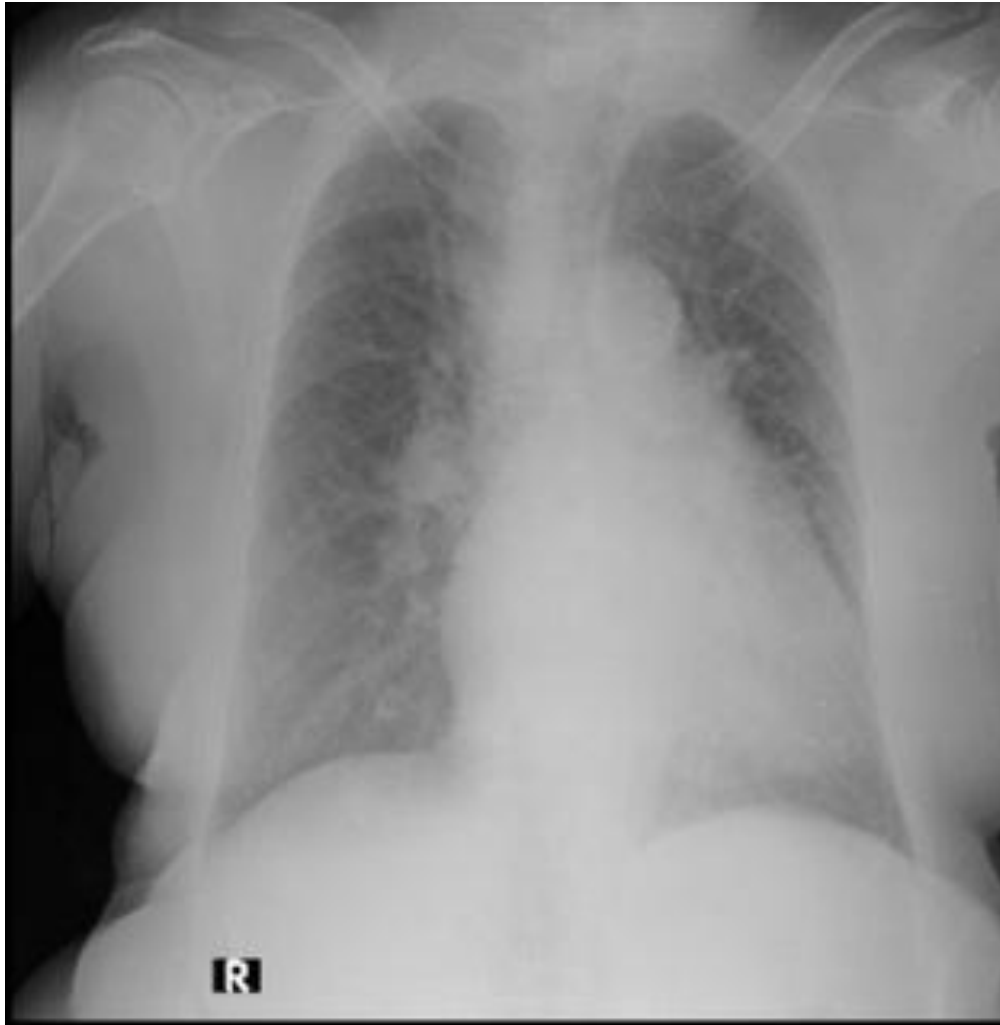


Figure 2. Chest x-ray showed pulmonary edema.

Then, patient was immediately given atropine up to a maximum cumulative dose of 12 ampoules (3 mg), but showed no chronotropic response. Intravenous aminophylline 240 mg was then administered. Following aminophylline administration, the heart rate increased significantly to 82 beats per minute (figure 3), followed by hemodynamic improvement and gradual resolution of pulmonary edema symptoms.

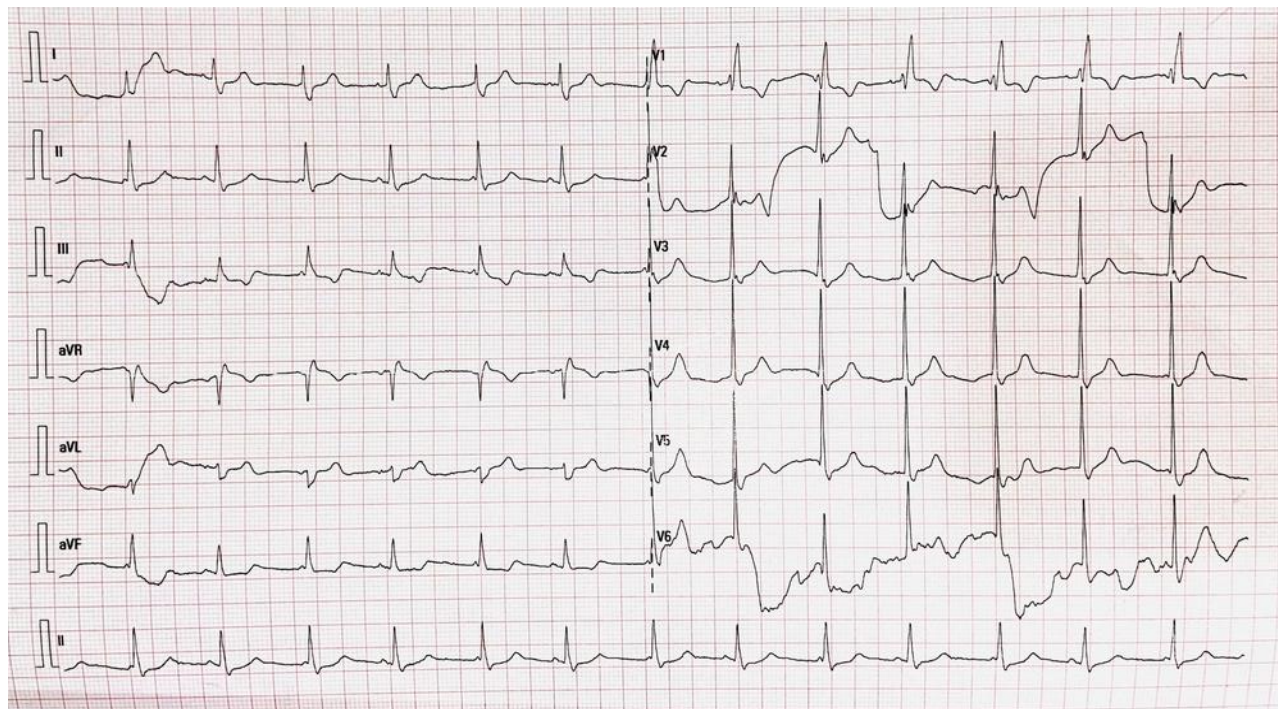


Figure 3. The ECG (after aminophylline administration) showed sinus rhythm with 82 beats/min.

DISCUSSION

In this case, the patient developed cardiogenic shock secondary to extreme bradycardia in the setting of acute-on-chronic kidney disease (ACKD), hyperkalemia, and pulmonary edema. The marked reduction in heart rate resulted in severe hemodynamic compromise, with pulmonary edema reflecting acute cardiopulmonary congestion.¹ In patients with ACKD, impaired renal function increases the risk of hyperkalemia. Elevated serum potassium can impair myocardial excitability and conduction, leading to conduction slowing, heart block, and bradycardia. Severe hyperkalemia may present with prominent bradyarrhythmias, and the response to atropine or pacing may be inadequate when the underlying electrolyte disturbance is not corrected.⁸

Adenosine signaling is also relevant to the regulation of cardiac rate and conduction. Adenosine acts through four receptor subtypes: A₁, A_{2A}, A_{2B}, and A₃. In the cardiovascular system, activation of the A₁ receptor suppresses sinoatrial node activity and slows atrioventricular

conduction, producing negative chronotropic and dromotropic effects. Adenosine signaling is involved in several cardiovascular conditions, including myocardial ischemia, myocardial infarction, arrhythmias, and heart failure.^{2,4} Therefore, adenosine-mediated effects may have contributed to the bradycardia in this patient. However, serum adenosine levels were not measured, and this mechanism therefore cannot be confirmed as the sole cause of the bradycardia.

The patient received atropine up to a total dose of 3 mg according to the recommended bradycardia algorithm, but the heart rate remained low.¹ Atropine is a parasympatholytic agent that inhibits parasympathetic effects on the heart, thereby increasing sinoatrial node automaticity and atrioventricular conduction. Its effects are particularly useful in bradycardia related to increased vagal tone or conduction abnormalities at the atrioventricular nodal level.⁶ The inadequate response to atropine in this case suggests that mechanisms other than increased parasympathetic activity also contributed to the bradycardia. In the setting of ACKD and hyperkalemia, hyperkalemia-induced impairment of myocardial excitability and conduction provides a plausible explanation for the persistent bradycardia and inadequate response to atropine.⁸

Aminophylline was subsequently administered as an alternative pharmacological treatment. Aminophylline is a methylxanthine with adenosine receptor antagonist and phosphodiesterase inhibitory activity. Its positive chronotropic effect is primarily attributed to antagonism of the suppressive effects of adenosine on the sinoatrial node, resulting in an increased heart rate.⁶ Aminophylline has also been reported as a treatment option for severe symptomatic bradycardia that is resistant to atropine.⁵ These pharmacological properties provide a rationale for considering aminophylline in selected patients with atropine-resistant bradycardia.

In this patient, aminophylline administration was followed by an increase in heart rate and improvement in hemodynamic status. This response demonstrates a positive chronotropic effect of aminophylline in this case and is consistent with its adenosine receptor antagonism.⁶ The clinical response, however, does not establish adenosine activity as the sole mechanism responsible for the bradycardia. Hyperkalemia, ACKD, and cardiogenic shock may also have contributed to the patient's electrophysiological and hemodynamic abnormalities. Thus, the response observed in this

case supports the positive chronotropic effect of aminophylline in a patient with complex bradycardia and an inadequate response to atropine.

Aminophylline also has phosphodiesterase inhibitory activity, which may contribute to its cardiovascular effects.⁶ However, the most relevant mechanism in this case is its positive chronotropic effect through adenosine receptor antagonism. Particular caution is required because the patient also had pulmonary edema. In patients with acute pulmonary edema, theophylline clearance may be reduced and its elimination half-life prolonged compared with patients without pulmonary edema. This may result in less predictable drug concentrations, particularly with repeated dosing or continuous infusion, and may increase the risk of toxicity.⁷ Therefore, aminophylline should be used cautiously in patients with pulmonary edema and impaired renal function, with consideration of the clinical condition and potential for drug accumulation.

Overall, this case demonstrates that in a patient with ACKD, hyperkalemia, and extreme bradycardia causing severe hemodynamic compromise, aminophylline was followed by an increase in heart rate and improvement in hemodynamic status after an inadequate response to atropine. This response is consistent with the positive chronotropic effect of aminophylline through adenosine receptor antagonism.⁶ The findings support consideration of aminophylline as a pharmacological option in selected patients with atropine-resistant bradycardia, while taking into account the underlying cause of bradycardia, hemodynamic status, renal function, and risk of drug toxicity.^{1, 5-7}

CONCLUSION

Aminophylline can be considered as an alternative treatment option for atropine-resistant bradycardia before the use of dopamine or epinephrine. In this case, its administration was followed by an increase in heart rate and improvement in hemodynamic status, supporting its potential role as an additional pharmacological option in selected patients.

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