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Effect of Aminophylline in Patients with Atropine-Resistant Late Advanced Atrioventricular Block during Acute Inferior Myocardial Infarction

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Summary

Background: Advanced atrioventricular (AV) block is a frequent complication in patients with acute inferior myocardial infarction (AIMI). This conduction abnormality is associated with narrow QRS complex in conducted or junctional escape beats, suggesting that the site of block is the AV node; however, its pathophysiology has not been properly established.

Hypothesis: This study investigated the effect of aminophylline in eight patients (5 men, 3 women, age range 51 to 78 years, mean 67.5 ± 8.8 years) with atropine-resistant late advanced AV block during AIMI.

Methods: Advanced AV block was late in appearance in all patients, starting 2 to 5 days after AIMI, and consisted of second-degree Mobitz II type in two patients and of complete AV block in six patients; all patients had narrow QRS complexes. Before aminophylline administration, all patients had a temporary pacemaker installed which was switched off throughout the study. They were given intravenous atropine (1 mg) that was found to be ineffective. One-half h after atropine, the first aminophylline injection (240 mg) was given intravenously over 10 min. One h following the first injection, a second aminophylline dose (240 mg) was administered. Electrocardiographic rhythm strips were obtained before and after drug administration, and the type of AV block and atrial and ventricular rate were noted.

Results: Aminophylline restored 1:1 conduction with first-degree AV block in six patients, Mobitz I AV block in one patient, and normal sinus rhythm in one patient. Mean atrial and ventricular rates before aminophylline were 104 ± 16 beats/min and 57 ± 9 beats/min, respectively, and after drug administration 95 ± 25 beats/min and 89 ± 17 beats/min, respectively, ($p = 0.012$).

Conclusion: These results indicate that aminophylline improves AV conduction in atropine-resistant late advanced AV block complicating AIMI.

Key words: aminophylline, advanced atrioventricular block, inferior myocardial infarction

Introduction

Advanced atrioventricular (AV) block is a frequent complication in patients with acute inferior myocardial infarction (AIMI).[1] This conduction abnormality is associated with narrow QRS complex in conducted or junctional escape beats, suggesting that the site of block is the AV node; however, its pathophysiology has not been properly established. Intravenous atropine often restores normal conduction, supporting the hypothesis that increased parasympathetic activity mediates the development of AV block.[2] However, the AV block may fail to respond to atropine, suggesting the presence of alternative mechanisms (acute ischemia and ischemic metabolites such as adenosine, potassium). Adenosine is an ischemic metabolite that depresses sinus node activity and impairs AV conduction.[3] Aminophylline is a competitive adenosine antagonist.

In this study, we investigated the effect of aminophylline in patients with atropine-resistant late AV block during AIMI.

Materials and Methods

Eight consecutive patients with AIMI who developed second-degree or complete AV block were included in this study (Table I). There were 5 men and 3 women with an age range from 51 to 78 years (mean 67.5 ± 8.8 years). Atrioventricular

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TABLE I Clinical characteristics and response to aminophylline

Patient No.	Age (years/sex)	AV block appearance (days)	Degree of AV block		Atrial rate		Ventricular rate	
			Before	After	Before	After	Before	After
1	69.F	5	Complete	1:1 PR: 0.56	110	98	64	98
2	70/F	4	Mobitz II 2:1 PR: 0.48	1:1 PR: 0.38	96	110	48	110
3	73/M	4	Complete	1:1 PR: 0.24	79	81	63	81
4	73/M	2	Mobitz II 2:1 PR: 0.24	1:1 PR: 0.24	120	100	60	100
5	78/M	4	Complete	1:1 PR: 0.24	100	60	44	60
6	58/M	2	Complete	1:1 PR: 0.16	100	100	48	100
7	68/F	2	Complete	Mobitz I 3:2/5:4	130	140	68	92
8	51/M	2	Complete	1:1 PR: 0.32	100	68	58	68
	67.5 ± 8.8				104 ± 16–95 ± 25 p = NS		57 ± 9–89 ± 17 p = 0.012	

Abbreviations: AV = atrioventricular, M = male, F = female, PR = PR interval (s), NS = not significant.

block was late, starting 2 to 5 days after the hyperacute stage of AIMI, and consisted of second-degree Mobitz II (2:1) in two patients and of complete AV block in six patients (Table I). All patients had narrow QRS complexes and no atrial fibrillation. It was necessary for patients to maintain a stable AV block rhythm for at least 1 h before aminophylline administration. Patients with AV block who were receiving drugs known to depress AV nodal conduction (e.g., digitalis, beta blockers, calcium-channel blockers) were excluded. Patients who developed AV block during the hyperacute phase of AIMI were also excluded because this early-appearing AV block tends to disappear abruptly and rapidly parallel to the disappearance of acute ischemia. Therefore, only patients with late advanced AV block were included.[4]

The diagnosis of AIMI was confirmed by medical history (chest pain lasting ≥ 30 min), unequivocal electrocardiographic (ECG) changes (new Q/QS and ST shifts with T changes) in the inferior leads, and high levels of serum cardiac enzymes.

Before aminophylline administration, all patients had a temporary pacemaker installed which was switched off throughout the study. All patients were given intravenous atropine (1 mg) that was found to be ineffective (no change in atrial rate, AV conduction, or ventricular rate over the next 15 min). One-half h after atropine, the first aminophylline injection (240 mg) dose was administered intravenously over 10 min. One h following the first aminophylline injection, a second aminophylline dose (240 mg) was administered. Patients were monitored throughout the study. Electrocardiographic rhythm strips were obtained before and every 10 min after drug administration, and the type of AV block, blood pressure, and atrial and ventricular rate were noted.

Results

There was no significant change in atrial rates (104 ± 16 beats/min vs. 95 ± 25 beats/min, respectively). Mean ventricular rate before aminophylline was 57 ± 9 beats/min and increased to 89 ± 17 beats/min after drug administration ($p = 0.012$). After the second aminophylline injection, AV conduction of the patients improved over the next 20 min (13.75 ± 5.18 min). Aminophylline restored 1:1 conduction with first-degree AV block in six patients, second-degree Mobitz I AV block in one patient, and normal sinus rhythm in one patient (Table I). No adverse effects were noted from the administration of aminophylline.

Systolic and diastolic blood pressures (119 ± 6 and 79 ± 8 mmHg, respectively) did not change after the first (120 ± 7 and 77 ± 4 mmHg) and the second (118 ± 3 and 76 ± 4 mmHg) aminophylline injections.

One h after the improvement of AV conduction, complete AV block occurred again in one patient (Patient No. 7). No further recurrence of AV block was observed in other patients during the in-hospital course.

Discussion

Advanced AV block is a frequent complication in patients with AIMI and has been reported in 9 to 34% of such patients.[1,5–12] Recently, we reported 258 patients with AIMI, of whom 21% had second- degree and complete AV block.[13] Several studies showed that patients with advanced AV block in AIMI have a higher incidence of congestive heart failure,

arrhythmias, and in-hospital mortality.[4, 7–10, 14–16] In our study, 18% of patients with advanced AV block in AIMI died during hospitalization.[13] These data are in accordance with previously published studies.[7–10, 14–16]

Some studies have classified AV blocks that occur during AIMI according to the time of their appearance (early vs. late block).[10, 14] These studies have shown contradictory results. Feigl *et al.*[10] reported that increased vagal tone is probably operative in the early block group, and metabolic changes due to ischemia in the late block group. For this reason, response to atropine and sympathomimetic drugs is much better and cardiac pacing is only rarely indicated in patients with early rather than late AV block.[10] However, Sclarovsky *et al.*[14] reported opposite results. They found that the early block group was characterized by short duration, complete AV block, poor response to atropine, and increased need for pacemaker therapy; the late block group was characterized by longer duration, second-degree type block, positive response to atropine, and diminished need for pacemaker therapy.[14]

Several potential mechanisms for the development of AV block in AIMI have been proposed, including increased parasympathetic activity, AV nodal ischemia, and release of ischemic metabolites (potassium, adenosine, etc.) in the vicinity of the AV node. During AIMI, activation of parasympathetic afferents in the inferoposterior wall of the left ventricle may cause reflex bradycardia, vasodilatation, and hypotension (the Bezold-Jarisch reflex), which is abolished by atropine.[2] Both Feigl *et al.*[10] and Sclarovsky *et al.*[14] did not exclude that increased parasympathetic activity mediates the development of AV block in their studies. Recently, we reported that the appearance of atropine-resistant AV block observed during the first 24 h of chest pain (early block) is related to severe and transient ischemia of the AV node, whereas atropine-resistant AV block occurring after the first 24 h of AIMI (late block) may be related to an increased release of ischemic metabolites, such as potassium and adenosine, that slow AV nodal conduction.[4]

Adenosine is a purine nucleoside the most prominent effect of which is impairment or blockade of AV nodal conduction, but other effects are depression of automaticity of the sinus node and attenuation of catecholamine-related ventricular afterdepolarizations.[3, 17, 18] The actions of adenosine are mediated via specific A_1 purinoceptors at the cardiac cell surface. Aminophylline is a competitive antagonist of these receptors and reverses the negative dromotropic effects of adenosine. For this reason, we investigated the effect of aminophylline in patients with atropine-resistant late advanced AV block during AIMI.

Some studies have tested the efficacy of aminophylline in reversing AV block in patients with late advanced AV block during AIMI. Wesley *et al.*[19] and Shah *et al.*[20] showed that aminophylline improved AV conduction in three patients with atropine-resistant late advanced AV block during AIMI. Wesley *et al.*[19] reported that sympathomimetic action of aminophylline might also contribute to the improvement of AV conduction. Strasberg *et al.*[21] reported that aminophylline did not improve AV conduction in patients with late advanced AV block complicating AIMI, but they did not exclude increased parasympathetic activity. Onodera *et al.*[22] showed that aminophylline restored AV conduction in two patients, but did not restore AV conduction in four patients with atropine-resistant late advanced AV block during AIMI. Their aminophylline dose was low (250 mg).

Conclusion

We found that aminophylline improves AV conduction in patients with atropine-resistant late advanced AV block during AIMI. The fact that, in this study, sinus node rate did not increase following the administration of aminophylline suggests that aminophylline reversed AV block without any sympathomimetic action. Perhaps a slight decrease in sinus node rate may be added to the improvement of AV conduction.

The findings in this study show that aminophylline, a competitive adenosine antagonist, can improve AV conduction in atropine-resistant late advanced AV block during AIMI, and therefore there will be a lesser need for temporary pacemaker therapy. Further studies are needed to elucidate the possible role of aminophylline in possible subgroups (e.g., administration of intravenous isoprenaline, hemodynamic unstable, slow ventricular rate) of atropine-resistant late advanced AV block.

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