Bradyarrhythmias Incident to Thrombolysis for Acute Inferior Wall Infarction*

A Caveat

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Of ten consecutive patients (eight men, two women; mean age, 59 years) seen over a ten-month period with acute inferoposterior infarction treated with thrombolytic therapy, seven patients demonstrated significant rhythm disturbances at a time interval consistent with clot lysis and in a setting of other clinical markers predictive of reperfusion. One patient had a ventricular arrhythmia treated with intravenous procaniamide, but six patients had marked bradyarrhythmias (sinus bradycardia, four patients; and 2° atrioventricular block, one patient) associated with hemodynamic compromise. Urgent treatment consisting of intravenous atropine sulfate (1 mg) briskly restored sinus rhythm and normal arterial pressure within 1 min. Bradyarrhythmias incident to thrombolysis for acute inferoposterior infarction appear to arise as a vagally mediated cardiovascular reflex (Bezold-Jarisch) and the rapid vagolytic effect of intravenous atropine sulfate makes this therapy specific and appropriate. (Chest 1992; 101:732-35)

AVR = accelerated idioventricular rhythm; rt-PA = recombinant tissue type plasminogen activator

METHODS

Patients

This study included all consecutive patients admitted to the Cabrini Medical Center of New York City over a ten-month period (February to December 1990) who were treated with thrombolytic therapy for acute inferior or inferoposterior infarction. Eligibility criteria for intravenous thrombolysis consisted of the following: (1) prolonged chest pain of at least 30 min and with a duration of less than 4 h or 6 h if pain remained severe and persistent; (2) an electrocardiogram (ECC) demonstrating acute inferior wall infarction in which ST segment elevation of at least 1.5 mm is present in the inferior leads (2, 3, aVF). Concomitant ST segment depression of at least 2 mm in two or more of the right precordial leads (V1 to V3) in the presence of acute inferior infarction was diagnosed as associated posterior wall infarction; and (3) age younger than 75 years.

Patients with myocardial infarction deemed ineligible for thrombolytic therapy were those with recent surgery, trauma, cerebrovascular disease, severe hypertension, active internal bleeding, bleeding diathesis, or prompt return of the ST segment to baseline after intravenous nitroglycerin. Informed consent was obtained from all patients.

Ten patients, eight men and two women, with an age range of 41 to 73 years (mean, 59 years), met these inclusion criteria for thrombolytic therapy. All patients had ECC evidence of sinus rhythm (rates between 60 and 80 beats/min) and acute inferior wall infarction; nine patients had concomitant ST segment depression in the right precordial leads consistent with associated posterior wall infarction. On examination, both arterial pressure and jugular venous pulse were normal in all patients; chest roentgenogram was free of pulmonary congestion. Five patients were receiving previous cardiac medication consisting of digoxin (one patient), nifedipine (one patient) and β-adrenergic blockers (three patients).

Treatment Design

Five patients received intravenous recombinant tissue type plasminogen activator (rt-PA), 10 mg bolus, followed by an infusion of 50 mg over 1 h and 40 mg over 2 h. Three patients received
anistreplase (APSAC), 30 U over 5 min. Two patients received streptokinase 1.5 million units over 1 h. All patients received 325 mg aspirin orally prior to thrombolytic therapy. Intravenous nitroglycerin was administered prior to thrombolytic therapy in all patients in doses ranging between 25 and 50 μg/min. No patient received morphine, other opiate medication, or β-blockers. Thrombolytic treatment was initiated in the emergency department approximately 1.5 to 4 h after onset of chest pain. All patients were then admitted to the coronary care unit for observation and ECG monitoring.

**Evaluation of Clinical Markers of Reperfusion**

An ECG was recorded 3 to 4 h after thrombolysis and the ST segment changes in the inferior leads (2, 3, aVF) were compared with the initial or baseline ST segment elevation in these same leads. A complete resolution of the initial ST segment shift or decrease in the sum of the ST segment deviation of 50 percent or more was considered a useful marker of reperfusion.

The prompt abatement or complete resolution of chest pain between 1.5 and 2 h after thrombolysis was also used as a clinical sign of reperfusion.5,7

**Reperfusion Arrhythmias**

All arrhythmias documented from ECG monitoring that occurred after the initiation of thrombolytic therapy at a time interval consistent with clot lysis (1 to 4 h) were considered to be incident and related to reperfusion of ischemic myocardium.

<table>
<thead>
<tr>
<th>Patient/ Age, yr/ Sex</th>
<th>Infarct Site</th>
<th>Thrombolytic Agent</th>
<th>Reperfusion Arrhythmia/ Blood Pressure</th>
<th>Therapy</th>
<th>Post-reperfusion Rhythm</th>
<th>Angiographic Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/63/M IIMI</td>
<td>Streptokinase</td>
<td>O/N</td>
<td>0</td>
<td>Sinus rhythm</td>
<td>3-vessel/RCA 90%</td>
<td></td>
</tr>
<tr>
<td>2/61/M IIMI/PMI</td>
<td>rt-PA</td>
<td>O/N</td>
<td>0</td>
<td>Sinus rhythm</td>
<td>II</td>
<td></td>
</tr>
<tr>
<td>3/45/M IIMI/PMI</td>
<td>rt-PA</td>
<td>Sinus bradycardia (20 BPM 2-s asystole 60 mm Hg palpable)</td>
<td>Atropine</td>
<td>Sinus rhythm 68 BPM</td>
<td>2-vessel/RCA 100%</td>
<td></td>
</tr>
<tr>
<td>4/71/M IIMI/PMI</td>
<td>Streptokinase</td>
<td>2° AV block (24 BPM 70/50 mm Hg)</td>
<td>Atropine</td>
<td>Sinus rhythm 76 BPM</td>
<td>III</td>
<td></td>
</tr>
<tr>
<td>5/50/M IIMI/PMI</td>
<td>rt-PA</td>
<td>Sinus bradycardia (28 BPM 80/60 mm Hg)</td>
<td>Atropine</td>
<td>Sinus rhythm 64 BPM</td>
<td>III</td>
<td></td>
</tr>
<tr>
<td>6/67/F IIMI</td>
<td>APSAC</td>
<td>O/N</td>
<td>0</td>
<td>Sinus rhythm</td>
<td>1-vessel/RCA 90%</td>
<td></td>
</tr>
<tr>
<td>7/62/F IIMI/PMI</td>
<td>rt-PA</td>
<td>Sinus bradycardia (24 BPM 3.5-s asystole 80/60 mm Hg</td>
<td>Atropine</td>
<td>Sinus rhythm 82 BPM</td>
<td>1-vessel/RCA 100%</td>
<td></td>
</tr>
<tr>
<td>8/60/M IIMI/PMI</td>
<td>APSAC</td>
<td>AIVR (70 BPM) ventricular tachycardia (150 BPM 110/70 mm Hg)</td>
<td>Procainamide</td>
<td>Sinus rhythm 58 BPM</td>
<td>III</td>
<td></td>
</tr>
<tr>
<td>9/41/M IIMI/PMI</td>
<td>rt-PA</td>
<td>Sinus bradycardia (30 BPM 2-s asystole 90/60 mm Hg)</td>
<td>Atropine</td>
<td>Sinus rhythm 68 BPM</td>
<td>2-vessel/RCA 90%</td>
<td></td>
</tr>
<tr>
<td>10/73/M IIMI/PMI</td>
<td>APSAC</td>
<td>Sinus bradycardia (22 BPM 6-s asystole 70 mm Hg palpable)</td>
<td>Atropine</td>
<td>Sinus rhythm 84 BPM</td>
<td>2-vessel/RCA 90%</td>
<td></td>
</tr>
</tbody>
</table>

Number of major epicardial coronary arteries with >75 percent stenosis/infarct artery with percent stenosis, *IIMI = inferior myocardial infarction; PMI = posterior myocardial infarction; o = absent; N = normal; BPM = beats per minute; AIVR = accelerated idioventricular rhythm; RCA = right coronary artery; rt-PA = recombinant tissue type plasminogen activator.

**Hospital Course and Angiographic Studies**

The hospital course was reviewed for complications, eg, congestive heart failure, hypertension, shock, angina, or subsequent arrhythmias. For those patients who consented, coronary arteriography was performed between the second and third week after infarction, and attention focused on the number of coronary vessels with occlusive disease and the specific findings of the infarct-related artery.

**RESULTS**

**Reperfusion Arrhythmias**

A manifest arrhythmia was documented in seven patients, 1 to 4 h after initiation of thrombolysis, and was considered to be causally related to coronary reperfusion. One patient had an idioventricular arrhythmia (70 beats/min) 4 h after initiation of thrombolysis that deteriorated after 15 min (see Table 1) to a rapid ventricular tachycardia (150 beats/min). Conversion to sinus rhythm was established after 400 mg of intravenous procainamide (Pronestyl) over a 10-min period followed by a 2-mg/min infusion. One patient demonstrated 2° atrioventricular (AV) block (ventricular rate 24 beats/min), associated marked hypotension 2 h after the onset of thrombolytic therapy. Sinus
rhythm and blood pressure were restored within 1 min after treatment with 1 mg of intravenous atropine sulfate. Five patients had the sudden appearance (1 to 2 h after thrombolytic therapy) of severe sinus bradycardia (rates ranging from 20 to 25 beats/min) associated with significant hemodynamic compromise. In four of these patients, sinus pauses ranging between 2 and 6 s were also recorded. All patients with reperfusion bradyarrhythmias received 1 mg of intravenous atropine sulfate within several minutes after the onset of the arrhythmias and both heart rate and blood pressure was restored to normal (see Table 1).

Clinical Markers of Reperfusion

The initial ST segment elevation in the inferior leads was completely resolved in three patients who had reperfusion arrhythmias within 4 h after thrombolytic therapy. In the other four patients who had reperfusion arrhythmias, the ST segment decreased to more than 50 percent of its initial elevation within the same time interval. In all seven patients who exhibited reperfusion arrhythmias, ischemic chest pain was completely resolved between 1.5 and 2 h after thrombolytic therapy was initiated.

Hospital Course and Angiographic Studies

Congestive heart failure or subsequent arrhythmias did not occur in any patient. Recurrent angina was noted in three patients. Coronary angiographic studies were recommended for eight patients, (two patients refused) who had either recurrent chest pain or reversible perfusion defects on exercise thallium scintigraphy.

Coronary angiographic studies were performed in six patients two to three weeks after hospital admission for infarction (see Table 1). Major coronary artery disease was reported when angiographic stenosis was >75 percent. Two patients had one-vessel disease and four patients had multivessel disease. The right coronary artery was identified as the infarct-related artery in all six patients. Of the four patients who had reperfusion bradyarrhythmias, the right coronary artery was totally blocked in two and 90 percent stenosed in two.

Discussion

Ventricular tachyarrhythmias, particularly accelerated idioventricular rhythm (AIVR) and nonsustained ventricular tachycardia, are commonly observed during thrombolytic therapy for acute myocardial infarction (AMI) and then tend to decline within 24 h after reperfusion. An increase in premature ventricular beats may also occur but this may be coincidental since this arrhythmia has a high prevalence in all patients with AMI. Many regard these ventricular arrhythmias, especially AIVR, as a marker of successful coronary recanalization, although this view is not shared by all. Ventricular arrhythmias after reperfusion are generally considered benign, even without antiarrhythmic therapy, since they rarely deteriorate into sustained ventricular tachycardia or ventricular fibrillation. It is postulated that these reperfusion arrhythmias arise from an electrically unstable ischemic zone rendered heterogeneous by changes in regional electrolyte concentration, α-adrenergic responsiveness, and washout of metabolites during reperfusion of blood flow.

Much less attention has been focused on the clinical significance and approach to bradyarrhythmias that arise in patients with acute inferoposterior infarction at the time of reperfusion. Sinus bradycardia and/or hypotension occur in the early phases, although transiently, of acute inferoposterior infarction and may be seen in the overwhelming majority of such patients. This phenomenon is attributed to ischemic stimulation of vagal efferent receptors preferentially distributed in the inferoposterior wall of the left ventricle and designated the Bezold-Jarisch reflex. During coronary artery reperfusion, particularly of the right coronary artery, this vagally mediated reflex may be reactivated.

Successful recanalization was noted in 27 patients by Wei et al after thrombolytic therapy for AMI. At the time of clot lysis, a significant bradycardia response and decline in arterial pressure were observed in those patients with right coronary artery reperfusion (n = 18) as compared with those patients with left coronary artery reperfusion (n = 9). In those patients (n = 11) with persistent occlusion of the infarct-related coronary artery, there were no reflex cardiovascular changes. In another report by Goldberg et al recanalization of an occluded right coronary artery was demonstrated in four of eight patients during intracoronary thrombolysis for AMI of the inferior wall. Marked bradyarrhythmias consisting of 2° AV block (n = 2) and sinus bradycardia (n = 2) in association with marked hypotension occurred at the time of reperfusion. Three patients required atropine sulfate to restore sinus rhythm and arterial pressure.

In our ten patients with acute inferoposterior infarction treated with reperfusion therapy, six patients manifested abruptly and without warning marked bradyarrhythmias (sinus bradycardia, five patients, and 2° AV block, one patient) associated with severe hemodynamic compromise at a time interval consistent with clot lysis. That these bradyarrhythmias were related to reperfusion was reinforced by two other clinical markers usually indicative of this phenomenon: prompt resolution of both chest pain, and ST segment elevation after thrombolytic therapy. Complete resolution of chest pain within 90 min of thrombolytic therapy in concert with ST segment resolution...
is considered to be highly predictive of successful reperfusion.6,7

This experience, although limited, suggests that bradyarrhythmias that emerge during reperfusion therapy for acute inferoposterior myocardial infarction may require urgent treatment. Intravenous atropine appears to be the most specific therapy since it abolishes the vagally mediated Bezold-Jarisch reflex responsible for these arrhythmias. Positive inotropes, vasoconstrictors, or temporary pacing as initial therapy in this setting may be inappropriate and even hazardous. It is of interest, although expected, that the right coronary artery was identified as the infarct-related artery in those angiographically studied patients with inferoposterior infarction. In four patients who manifested reperfusion bradyarrhythmias, the right coronary artery, although patent in two patients, was totally blocked in the other two patients due presumably to reoclusion.

REFERENCES
11 Wei JY, Markis JE, Malagold M, Brunwald E. Cardiovascular reflexes stimulated by reperfusion of ischemic myocardium in acute myocardial infarction. Circulation 1983; 67:796-801