Use of Atropine in Patients with Acute Myocardial Infarction and Sinus Bradycardia

By Melvin M. Scheinman, M.D., David Thorburn, and Joseph A. Abbott, M.D.

SUMMARY
Fifty-six patients with acute myocardial infarction complicated by sinus bradycardia (SB) were treated with intravenous atropine and monitored in a coronary care unit. Atropine decreased or completely abolished premature ventricular contractions (PVCs) and/or bouts of accelerated idioventricular rhythm in 27 of 31 patients (87%) and brought systemic blood pressure up to normal in 15 of 17 patients (88%) with hypotension. In addition, atropine administration was associated with improved atrioventricular conduction in 11 of 13 patients (85%) with acute inferior myocardial infarction associated with 2o or 3o atrioventricular block. Seven patients developed ten significant adverse effects: ventricular tachycardia or fibrillation in three, sustained sinus tachycardia in three, increased PVCs in three, and toxic psychosis in one. These major adverse effects correlated with either a higher initial dose of atropine (i.e., 1.0 mg as compared with the usual 0.5 or 0.6 mg) or a total cumulative dose exceeding 2.5 mg over 24 hours. Atropine is the drug of choice for management of patients with SB and hypotension and is effective in the treatment of ventricular arrhythmias as well as conduction disturbances in patients with inferior myocardial infarction. Serious adverse effects, however, preclude use of atropine without careful medical supervision.

ATROPINE has been suggested as the treatment of choice for hypotension and/or premature ventricular depolarizations (PVCs) in patients with acute myocardial infarction and bradycardia.1'4 Recent laboratory studies,5, 6 however, have emphasized the possible adverse effects of atropine in the presence of acute myocardial ischemia, and several reports have extended these observations to patients with acute myocardial infarction.8, 10 Although previous studies have carefully documented the incidence and mortality associated with sinus bradycardia,11-13 no detailed evaluation of the benefits and hazards of atropine therapy in patients with acute myocardial infarction under continuous electrocardiographic monitoring in a coronary care unit is available. Such an evaluation is reported here.

Materials and Methods
Data from all patients admitted to the coronary care unit at San Francisco General Hospital with the diagnosis of definite acute myocardial infarction from July, 1970, to July, 1974, were reviewed. Our criteria for the diagnosis of definite acute myocardial infarction were described in detail previously.14 In brief, they consist of a compatible history, evolutionary electrocardiographic changes, and characteristic changes of serum creatine phosphokinase (CPK), glutamic oxaloacetic transaminase (SGOT), and lactate dehydrogenase (LDH) levels. From July, 1973, to December, 1974, the MB fraction of the serum CPK was also used to confirm the diagnosis.15 All patients were under continuous electrocardiographic monitoring, including a 12 sec memory tape automatically triggered by preset alarms. All rhythm strips were inserted into the medical record. Patients with sinus bradycardia (defined as heart rate below 60 beats/min) were included in the study. Excluded from the study were patients with sinus bradycardia occurring preterminally or appearing during or after cardiopulmonary resuscitation, patients with anterior myocardial infarction with sinus bradycardia and atrioventricular (A-V) block because they were treated with emergency insertion of a temporary transvenous pacemaker, patients who received medications that could conceivably affect heart rate (e.g., digitalis, propranolol), or patients with known antecedent sinus bradycardia. The majority of patients received analgesics (usually morphine) before admission to the coronary care unit, and the incidence of sinus bradycardia did not differ significantly between those who received analgesics (29%) and those who did not (28%). Patients admitted to the coronary care unit were treated by house officers under the supervision of a single attending physician (M. M. Scheinman). During the study period, the unit policy was to treat all patients with acute myocardial infarction complicated by sinus bradycardia and pump failure with an initial bolus intravenous injection of at least 0.5 mg of atropine sulfate. Patients with acute myocardial infarction, sinus bradycardia, and ventricular arrhythmias were treated with either atropine or antiarrhythmic agents; the choice of drug and dose were left to the discretion of the house officer. In those patients who received atropine, the dose of drug and time intervals between doses were recorded. In addition, continuous electrocardiographic rhythm strips were obtained before and for 3 min after
Beneficial and Adverse Effects Associated with Administration of Atropine in Patients with Acute Myocardial Infarction and Sinus Bradycardia

<table>
<thead>
<tr>
<th>Event</th>
<th>Incidence</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decrease or abolition of ventricular arrhythmias</td>
<td>27/31 (87%)</td>
<td>15/17 (88%)</td>
</tr>
<tr>
<td>Normalization of pressure in hypotensive patients</td>
<td>11/13 (85%)</td>
<td></td>
</tr>
<tr>
<td>Improvement in A-V conduction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sustained sinus tachycardia</td>
<td>3/56 (5%)</td>
<td></td>
</tr>
<tr>
<td>Increased number of PVCs</td>
<td>3/56 (5%)</td>
<td></td>
</tr>
<tr>
<td>Ventricular tachycardia or fibrillation</td>
<td>3/56 (5%)</td>
<td></td>
</tr>
<tr>
<td>Toxic psychoses</td>
<td>1/56 (1.8%)</td>
<td></td>
</tr>
</tbody>
</table>

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pari passu with the increased atrial rate after atropine. In two patients whose rhythm strips showed 3:2 and 4:3 A-V Wenckebach conduction, atrial rate increased with 2:1 and 3:2 Wenckebach conduction after atropine; ventricular rate and blood pressure also increased after atropine in these patients. Rhythm strips of seven patients showed A-V dissociation due to complete A-V block that reverted to 1:1 A-V conduction after atropine; however, sustained sinus tachycardia with 1:1 A-V conduction resulted in ventricular tachycardia in one and ventricular fibrillation in another (see above).

Systemic Blood Pressure

For the group as a whole, mean cuff systemic blood pressure rose from 107 ± 30/69 ± 18 before atropine to 127 ± 23/80 ± 18 mm Hg after atropine. In 17 patients with systemic hypotension (systolic pressure < 100 mm Hg), mean blood pressure rose significantly (P < 0.05) from 77 ± 17/43 ± 20 to 115 ± 12/69 ± 12 mm Hg. Seven of these patients had evidence of decreased systemic flow manifested by cool clammy skin and altered sensorium; these clinical manifestations were dramatically reversed within minutes after atropine. Two of the 17 patients with hypotension failed to respond to atropine but were successfully managed with low dose isoproterenol infusions.

### Atropine Dose and Major Adverse Effects

Single bolus injections of atropine varied from 0.5 to 1.0 mg. Absolute or mean percent increase in heart rate did not differ significantly in patients who received 0.5 or 0.6 mg (+32 beats/min), 0.8 mg (+27 beats/min), or 1.0 mg atropine (+55 beats/min). Ten instances of major adverse effects of atropine were observed in seven of the 56 patients treated (fig. 1): sustained (>5 min) sinus tachycardia developed on three occasions, more frequent PVCs occurred in three, ventricular tachycardia or fibrillation occurred in three, and toxic psychosis developed in one. Major adverse effects occurred in two of 34 patients (5%).

<table>
<thead>
<tr>
<th>Major adverse effect (No. of occurrences)</th>
<th>No. of occurrences and initial atropine dose</th>
<th>No. of occurrences and cumulative dose 2.5 mg in 2.5 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sustained sinus tachycardia (3)</td>
<td>1*</td>
<td>1</td>
</tr>
<tr>
<td>More frequent PVCs (3)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Ventricular tachycardia or fibrillation (3)</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Toxic psychosis (1)</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>Total (10)</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

*These patients are the same subjects who developed ventricular tachycardia or fibrillation.

![Figure 2](image1.png)

**Figure 2**

Electrocardiographic recordings (using modified V1 or MCL leads) of a patient with sinus bradycardia. A) before atropine, sinus bradycardia with a heart rate of 42 beats/min. B) after administration of 1.0 mg atropine intravenously, sinus tachycardia with a peak ventricular rate of 150 beats/min developed and was sustained for 5 min without change in blood pressure or clinical status. Lidocaine infusion for treatment of ventricular quadrigeminy had been started before atropine administration.

![Figure 3](image2.png)

**Figure 3**

Electrocardiographic recordings of a patient with sinus bradycardia associated with PVCs. A) before atropine, sinus bradycardia (80 beats/min) and coupled PVCs with the second beat of the pair interrupting the preceding T wave were present. B) after administration of 0.5 mg atropine intravenously, normal sinus rhythm with a heart rate of 63 beats/min occurred and PVCs were abolished.
who received an initial dose of 0.6 mg and four of 15 (26%) who received an initial dose of 1 mg (table 2). All patients (four) who received greater than 2.5 mg within 2½ hours developed major adverse effects. The amount of atropine required for maintenance of a ventricular rate between 70 to 100 beats/min was extremely variable: normal heart rates were achieved after one dose of 0.5 to 1.0 mg of atropine in 27 patients, whereas multiple doses with the total dose ranging from 1.0 to 8.0 mg were required in 29 patients. One patient received 1 mg of atropine every 6 hours for 48 hours; each dose resulted in acceleration of the sinus rate and abolition of an accelerated idioventricular rhythm.

Discussion

Atropine and Ventricular Arrhythmias

Our study confirms the effectiveness of intravenous administration of atropine in abolishing either sporadic PVCs and/or accelerated idioventricular rhythms in patients with acute myocardial infarction and sinus bradycardia. However, recent case reports emphasized the association between development of serious ventricular dysrhythmias and atropine administration in patients with these disorders. Moreover, Epstein and colleagues showed that bradycardia produced by vagal stimulation was associated with a reduced incidence of serious ventricular arrhythmias and an increased threshold for ventricular fibrillation in the canine preparation with myocardial ischemia. In addition, they found that only PVCs closely coupled to the preceding ventricular complex (<0.43 sec) were associated with serious ventricular dysrhythmias and that atropine effectively abolished most PVCs with longer coupling intervals but rarely abolished closely coupled PVCs.

In our study, only one of three patients (fig. 3) with frequent PVCs and short coupling intervals responded to atropine therapy; the small number of patients with PVCs associated with short coupling intervals precludes meaningful comparison with previous data obtained in the canine model. However, there is an apparent difference between the effects of myocardial ischemia in man and dog with respect to the relationship of the PVC coupling interval and the development of more serious ventricular arrhythmias. De Soyza et al. found in patients with acute myocardial infarction that the mean coupling interval between PVCs initiating serious ventricular arrhythmias (0.59 ± 0.14 sec) did not differ significantly from the interval in patients who did not develop more serious ventricular arrhythmias (0.55 ± 14 sec). In their report, 15% of the episodes of paroxysmal ventricular tachycardia occurred at sinus rates below 60 beats/min, but unfortunately, the number of episodes preceded by PVCs with long coupling intervals was not given.

Although previous studies have shown that late
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The administration of atropine may be associated with ventricular arrhythmias in both dogs and man, the malignant potential of such PVCs in patients with acute myocardial infarction and sinus bradycardia is unknown. In view of this uncertainty, the clinician must carefully evaluate the possible risks associated with these PVCs compared with the possible adverse effects associated with any of the currently available therapeutic regimens. Furthermore, our observations that increased heart rate almost always reduced or abolished PVCs in patients with acute myocardial infarction tend to support the experimental observations of Han et al., who found that the incidence of PVCs diminished with increased ventricular rate in dogs with myocardial ischemia. In addition, Chadda et al. found that in dogs with myocardial ischemia a heart rate between 110 to 150 beats/min was associated with a lower incidence of PVCs and/or more serious ventricular arrhythmias. Conclusions based on studies of myocardial ischemia in the open-chest dog model (with the attendant changes in autonomic tone) must, of course, be applied with caution to clinical situations.

Finally, although accelerated idioventricular rhythms appear to be transient and benign in the vast majority of patients with acute myocardial infarction, isolated reports have shown that these rhythms may, in fact, deteriorate into more serious ventricular dysrhythmias. In our study, the accelerated idioventricular rhythms associated with sinus bradycardia almost always responded to atropine therapy.

Bradyarrhythmia-Hypotension Syndrome

Twenty percent (17 of 83) of the patients had associated hypotension, and the incidence of this complication was especially high, 8 or 13 (61%), in patients with associated A-V block. Seven of the 17 patients with hypotension (41%) had clinical manifestations of severe impairment in systemic flow. Intravenous administration of atropine resulted in a prompt and often dramatic rise in arterial pressure in all but two patients. Our observations confirm previous reports of the beneficial effects of atropine in the prehospital phase, as well as in the hospital management of patients with this syndrome. The prompt reversal of both hypotension and impaired blood flow suggests that atropine blocks an increase in vagal tone that may be initiated from primary cardiac receptors. Although the increased heart rate produced by atropine may result in increased myocardial oxygen need and extension of myocardial ischemia (and/or further electrical instability), the rise in systemic blood pressure would be expected to counteract these effects by increasing coronary perfusion.

Adverse Effects of Atropine Administration

Although our studies confirm the beneficial effects of atropine in patients with acute myocardial infarction and sinus bradycardia complicated by either PVCs and/or hypotension, the effects of atropine are not totally benign (table 2). Transient sinus tachycardia and/or minor side effects characteristic of parasympatholysis developed in approximately 20% of our patients treated with atropine. Ten serious adverse effects developed in seven patients, including ventricular tachycardia or fibrillation on three occasions. Similarly, there were three instances of increased PVCs and three of sustained sinus tachycardia after atropine. The initiation of increased ventricular irritability was not necessarily preceded by sinus tachycardia. For example, in one patient (fig. 5) PVCs and ventricular fibrillation occurred after increases in heart rate that were still within the normal range.

Finally, toxic psychosis, probably related to excessive atropine dosing, occurred in one patient.

Recommended Usage of Atropine

Review of the literature reveals widely differing recommendations regarding the dosage schedule of atropine for patients with acute myocardial infarction and bradycardia. We believe that our own observations offer useful guidelines for atropine dosing in patients with acute myocardial infarction. We found no significant difference between the increments in heart rate and blood pressure in patients receiving an initial dose of either 0.5 or 0.6 mg compared with those receiving 1.0 mg. On the other hand, the incidence of major adverse effects was lower (5%) in those receiving the lower dose than in those receiving 1.0 mg (26%). It must be appreciated that the lower dose does not completely protect the patient from serious adverse effects, but our experience suggests that such effects are much less frequent when smaller initial doses are used. In addition, all patients who received greater than 2.5 mg of atropine within the first 2½ hours had major untoward effects, accounting for 40% of the major adverse effects noted. Our data suggest intravenous administration of 0.5 or 0.6 mg of atropine initially followed by incremental doses of 0.5 mg in order to treat the specific indications listed below but not to exceed a total dose of 2.5 mg within 2½ hours.

The clinician must carefully weigh the risk/benefit ratio in the use of atropine in patients with acute myocardial infarction complicated by bradyarrhythmias. Our observations led us to the following additional conclusions. 1) Atropine administration is the drug of choice in the treatment of patients with sinus bradycardia and hypotension. It almost always results in increases in both heart rate and blood pressure, especially in patients with sinus bradycardia and aten-
dant A-V block. 2) The PVCs occurring in patients with acute myocardial infarction and sinus bradycardia are usually effectively abolished by atropine. These benefits must be weighed against the potential adverse effects of sinus tachycardia and serious ventricular arrhythmias, especially in modest sinus bradycardia associated with late coupled PVCs, because the malignant potential, if any, of this arrhythmia is presently unknown. We believe that atropine can be used safely in patients with acute myocardial infarction, provided proper attention is paid to atropine dosing, in a coronary care setting in which the adverse effects may be reversed. Unsupervised self-administration of this agent exposes the patient to a risk of potentially serious adverse effects.

3) Atropine should not be administered to patients with sinus bradycardia without ventricular irritability, hypotension, or evidence of pump failure. These patients usually have a benign clinical course.

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