Effect of Dopamine on Hemodynamics and Myocardial Metabolism in Shock Following Acute Myocardial Infarction in Man

HILTRUD S. MUELLER, M.D., ROBERT EVANS, B.A., AND STEPHEN M. AYRES, M.D.

SUMMARY Eight patients in shock associated with acute myocardial infarction were treated with dopamine. We titrated the dopamine dose to increase mean arterial pressure to 65–70 mm Hg and urine output to greater than 40 ml/hr. Increase of heart rate to 120–125 beats/min and occurrence of potentially dangerous arrhythmias were limiting endpoints. Dopamine administration increased 17.2 µg/kg/min. Heart rate increased from 95 to 118 beats/min (P < 0.001), and mean arterial pressure rose from 60 to 65 mm Hg (P < 0.05). Dopamine increased myocardial contractility as indicated by increase in cardiac index and systolic ejection rate, with only moderate decrease in systemic vascular resistance. Pulmonary wedge pressure and right atrial pressure decreased from 23 to 18 mm Hg (P < 0.05) and from 10 to 8 mm Hg (P < 0.01) respectively. Improvement in hemodynamic status by dopamine was associated with deterioration of myocardial metabolism. Myocardial oxygen extraction ratios and arterial-coronary sinus oxygen differences increased from 73 to 76% (P < 0.05) and from 13.02 to 14.19 ml/100 ml (P < 0.02) respectively. Myocardial lactate production increased from −8 to −15% (P = 0.05).

We conclude that dopamine improved cardiac performance at the expense of myocardial oxygenation and that dopamine is potentially harmful to acutely ischemic myocardium.

AN INTRODUCTION OF DOPAMINE INTO CLINICAL MEDICINE arose from the recognition that the agent had unique effects on the peripheral circulation. Earlier studies with that sympathomimetic amine, the immediate precursor of L-norepinephrine, suggested that it had mixed alpha and beta adrenergic stimulating properties and closely resembled epinephrine in its pharmacologic activity.¹⁻⁴ This view was challenged by a number of investigators who showed that, unlike epinephrine, dopamine had a selective vasodilating effect on certain vascular beds due to action on specific dopamine receptors.⁵⁻⁸ Dopamine-induced vasodilatation, not abolished by propranolol, was shown in the renal, mesenteric, coronary and cerebral vascular beds but not in the denervated skeletal muscle vasculature.¹⁹ The vasodilatation was selectively antagonized by phenothiazines and butyrophenones.¹¹⁻¹³

Our own studies and those of others have emphasized that the choice of a vasoactive agent in the critically ill patient frequently requires balancing cardiac and peripheral effects,⁹⁻¹⁰ particularly in patients with decreased coronary reserve. Beta-adrenergic stimulation by isoproterenol improves myocardial contractility and cardiac output but frequently increases myocardial oxygen requirements beyond that available. Alpha-adrenergic stimulation by L-norepinephrine raises coronary perfusion pressure and enhances oxygen delivery to myocardium supplied by diseased coronary arteries, but reduces peripheral blood flow. Dopamine has been shown to maintain central aortic pressure at the same time that it augments renal and splanchnic perfusion by direct dilatation of those vascular beds.

This paper presents the effects of dopamine on the hemodynamic status and on myocardial metabolism in eight patients in shock associated with acute myocardial infarction. The study indicates that dopamine in the doses needed to increase peripheral perfusion and arterial blood pressure in these patients markedly increased myocardial oxygen consumption and led to deterioration of myocardial metabolism. For this reason, dopamine is potentially harmful to acutely ischemic myocardium.

Methods

Patients were considered for the present study if the criteria for left ventricular pump failure following acute myocardial infarction were present; a) absent or poor peripheral pulses; b) cold, clammy skin; c) intravascular
arterial systolic pressure below 85 mm Hg; d) pulmonary artery wedge pressure above 18 mm Hg; e) urine output per hour less than 25 ml; f) electrocardiographic findings of acute transmural myocardial infarction evidenced by development or presence of Q waves and of acute elevation of ST segments; g) history characteristic of acute infarction; h) increased serum content of creatine kinase and its isoenzyme MB.

The protocol for hemodynamic and metabolic evaluation was approved by the human experimentation committee. Informed consent was obtained from the patient or relatives after explaining the purpose of the evaluation and the placement of catheters. Emergency therapy was instituted. Metabolic acidosis was treated with intravenous administration of bicarbonate aiming for a concentration above 20 mEq/L in the arterial blood. Prior to the control study, the bicarbonate contents averaged 21 mEq/L (range 17–25). The arterial oxygen tension was maintained above 85 mm Hg. Three of the eight patients were placed on a volume cycled respirator. Diazepam and phenobarbital were administered as needed to facilitate assisted ventilation.

A #7 Swan-Ganz thermodilution catheter was advanced into the pulmonary artery and a #7 Goodale Lubin catheter into the mid-portion of the coronary sinus. A #10 teflon catheter was placed into the brachial or axillary artery via puncture of the surgically exposed radial artery. Cardiac output was determined in triplicate by thermodilution technique. Details about sampling techniques, determination of plasma concentrations of lactate, pH, of oxygen and carbon dioxide tensions have been previously published.14 Table 1 presents the reproducibility of metabolic determinations in our laboratory. Plasma free fatty acids were measured by the method of Dole,16 modified by Trout et al.,17 and Mosingler.18 Blood oxygen and carbon dioxide contents were determined by the Van Slyke method.19 The Student's t-test for paired data was used for statistical analysis.20

Studies were performed before and during constant infusion of dopamine, approximately after 20 min of drug infusion to achieve a relatively stable heart rate and mean arterial pressure. Our aims for dopamine titration were 1) increase in mean arterial pressure to 65–70 mm Hg and 2) increase in urine output above 40 ml/hr. Drug infusions were decreased or discontinued if heart rate rose above 120–125 beats/min or if potentially dangerous arrhythmias were observed. Arrhythmias were considered as potentially dangerous if premature contractions occurred with frequency of 10 or more (atrial origin) or 6 or more (ventricular origin) per minute, if they occurred as bigeminy, in salvos of 2 or more or from different foci. The dopamine dose administered averaged 17.2 µg/kg/min (range 8.2 to 26.1).

Calculation of Derived Data

Systemic vascular resistance, SVR, (dynes-sec-cm–4) = mean arterial pressure minus right atrial pressure times 79.9 divided by cardiac output. Systolic ejection period, SEP (sec/beat) = interval between onset of the rise in arterial pressure and the incisura. The interval was measured from the tracing obtained at 100 mm/sec paper speed from the proximal brachial or distal axillary artery. Systolic ejection rate, SER, (ml/sec/M3) = stroke index divided by systolic ejection period. Myocardial extraction

### Table 1. Reproducibility of Metabolic Determinations

<table>
<thead>
<tr>
<th>Measurement</th>
<th>N</th>
<th>Coefficient of Variation, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactate content, mM/L</td>
<td>25</td>
<td>2.50</td>
</tr>
<tr>
<td>Free fatty acid content, µM/L</td>
<td>20</td>
<td>1.71</td>
</tr>
<tr>
<td>Oxygen content (Van Slyke), ml/100 ml</td>
<td>25</td>
<td>1.04</td>
</tr>
<tr>
<td>Carboxide content (Van Slyke), ml/100 ml</td>
<td>25</td>
<td>0.54</td>
</tr>
<tr>
<td>Oxygen tension, mm Hg</td>
<td>20</td>
<td>0.90</td>
</tr>
<tr>
<td>Carbon dioxide tension, mm Hg</td>
<td>20</td>
<td>1.23</td>
</tr>
<tr>
<td>pH</td>
<td>20</td>
<td>0.14</td>
</tr>
</tbody>
</table>

ratio, Ex, (%) = arterial-coronary sinus difference divided by arterial content.

### Results

Eight patients, seven men and one woman, were studied 6–18 hours after development of the shock state, 12 hours to 3 days after clinical onset of acute myocardial infarction. Treatment was initiated as soon as the patient arrived in the Intensive Coronary Care Unit. The average age was 63 years and ranged from 53–69 years. The electrocardiogram revealed anterior wall infarction in four, anterior-lateral wall infarction in two, and inferior and inferior-posterior wall infarction in two. In three instances, an old myocardial infarction was documented by electrocardiogram. Plasma peak creatine kinase averaged 2638 units/L (range 1610–3400) and peak isoenzyme MB averaged 348 units/L (range 180–520). Initial arterial concentrations of free fatty acids averaged 1408 µM/L (range 920–2400), of lactate 5.03 mM/L (range 3.56–6.91), and of glucose 293 mg/100 ml (range 187–398).

### Results of Initial Measurements of Hemodynamics and Myocardial Metabolism

Mean values are shown in table 2, individual measurements in figures 1 and 2. Heart rate ranged from 70–112 beats/min and arterial pressure from 72–83 mm Hg systolic, 48–56 mm Hg diastolic, and 57–65 mm Hg mean. Right atrial pressure varied between 7 and 14 mm Hg and pulmonary wedge pressure between 18 and 29 mm Hg. Cardiac index and arterial-pulmonary artery oxygen difference ranged from 1.30–1.97 L/min/M2 and 5.98–8.10 ml/100 ml respectively. Systemic vascular resistance ranged from 1540 to 2280 dynes-sec-cm–4.

Myocardial oxygen extraction ratios (Exo2)* and arterial-coronary sinus oxygen differences (A-CS)2* were abnormally high in seven of the eight patients ranging from 69–77% and from 11.53 to 15.84 ml/100 ml respectively. Coronary sinus oxygen tensions (CSPO2) averaged 22 mm Hg, the pH 7.26 units. Myocardial lactate production ranging from −5 to −16% was observed in six of eight patients, myocardial lactate extraction (ExL)* of 2 and 6% was seen in the remaining two. Myocardial free fatty acid extraction varied between 2 and 9%.

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*Normal values in our laboratory: mean ± 3(S D)N = 20

Exo2, % = 64 ± 3.69

CSPO2, mm Hg = 26 ± 3.19

(A–CSPO2) ml/100 ml = 10.22 ± 1.10

ExL, % = 24 ± 4.75
**Table 2. Effects of Dopamine on Hemodynamics and Myocardial Metabolism**

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Mean ± SD, N = 8</th>
<th>Control</th>
<th>Dopamine</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats/min)</td>
<td></td>
<td>95 ± 13.9</td>
<td>118 ± 11.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Arterial pressure (mm Hg)</td>
<td></td>
<td>78 ± 4.24</td>
<td>97 ± 7.50</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Arterial diastolic pressure (mm Hg)</td>
<td></td>
<td>52 ± 2.45</td>
<td>55 ± 5.55</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Arterial mean pressure (mm Hg)</td>
<td></td>
<td>60 ± 3.31</td>
<td>65 ± 5.81</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Cardiac index (L/min/M²)</td>
<td></td>
<td>1.64 ± 0.22</td>
<td>2.20 ± 0.27</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Arterial-pulmonary artery oxygen difference (ml/100 ml)</td>
<td></td>
<td>6.84 ± 0.79</td>
<td>5.67 ± 0.68</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systemic vascular resistance (dynes-sec-cm⁻⁴)</td>
<td></td>
<td>1786 ± 243</td>
<td>1483 ± 120</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Systolic ejection rate (ml/sec/M²)</td>
<td></td>
<td>68 ± 9.46</td>
<td>88 ± 6.03</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Right atrial pressure (mm Hg)</td>
<td></td>
<td>10 ± 2.50</td>
<td>8 ± 2.38</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Pulmonary wedge pressure (mm Hg)</td>
<td></td>
<td>23 ± 3.96</td>
<td>18 ± 2.39</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Myocardial oxygen extraction (%)</td>
<td></td>
<td>73 ± 2.45</td>
<td>76 ± 3.20</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Arterial-coronary sinus oxygen difference (ml/100 ml)</td>
<td></td>
<td>13.02 ± 1.78</td>
<td>14.19 ± 1.97</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Myocardial lactate extraction (%)</td>
<td></td>
<td>-8.39 ± 9.29</td>
<td>-15.10 ± 16.15</td>
<td>=0.05</td>
</tr>
<tr>
<td>Myocardial free fatty acid extraction (%)</td>
<td></td>
<td>5.88 ± 2.33</td>
<td>5.75 ± 5.47</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Effect of Dopamine on Hemodynamic Status and on Myocardial Metabolism**

Figure 1 shows that heart rate increased during dopamine administration in all patients; the mean changed from 95 to 118 beats/min. Systolic and mean arterial pressures increased in all but two patients, the averages from 78 to 97 mm Hg and 60 to 65 mm Hg respectively (see table). Cardiac index uniformly increased, the average 0.56 L/min/M². This increase of cardiac index was associated with a fall of the arterial-pulmonary artery oxygen difference, from an average of 6.84 to 5.67 ml/100 ml. Systemic vascular resistance decreased in six patients and remained essentially unchanged in two, the average changed from 1786 to 1483 dynes-sec-cm⁻⁴. Right atrial and pulmonary wedge pressures decreased from an average of 10 to 8 mm Hg and 23 to 18 mm Hg respectively. Systolic ejection rate increased an average of 28%. Atrial and ventricular irritability was enhanced or occurred in three of the eight patients and dopamine administration was stopped in one patient and dosage decreased in two. Urine output increased from an average of 20 to 76 ml/hr.

Myocardial oxygen extraction ratios (fig. 2) and arterial-coronary sinus oxygen differences increased in six patients, remained essentially unchanged in one and decreased in one patient. The averages changed from 73 to 76% (P < 0.05) and from 13.02 to 14.19 ml/100 ml (P < 0.02) respectively (see table). Figure 2 demonstrates that the rate of myocardial lactate production increased in five of six patients producing lactate and remained unchanged in one. In two patients, lactate extraction remained below 10%. The average lactate extraction ratio changed from -8 to -15%. Myocardial free fatty acid extraction varied but remained low during dopamine infusion. Four patients decreased free

**Figure 1. Effect of dopamine on hemodynamic status. Results in individual patients are shown prior to and during dopamine infusion. Heart rate and cardiac index uniformly increased. Changes in mean arterial pressures were moderate.**

**Figure 2. Effect of dopamine on myocardial metabolism. Oxygen extraction increased in 6 patients, decreased in 1 and remained essentially unchanged in 1 patient. The rate of lactate production increased in 5 instances and did not change in one. In three of the four patients, decreasing free fatty acid extraction, lactate production was enhanced; it was unchanged in 1 patient.**
fatty acid extraction. In three of these patients the rate of lactate production increased; it remained unchanged in one patient. Five of the eight patients received dopamine until intra-aortic counterpulsation was initiated (1–5 hours). After hemodynamic stabilization, heart catheterization and aortocoronary bypass surgery were performed. Four patients were discharged and are relatively well with mild restriction of activity. One patient died following surgery in a low cardiac output state. Three of the eight patients were not eligible for cardiac assistance because of gross cardiac enlargement and previous left ventricular failure. Dopamine temporarily improved the shock state; two succumbed in the hospital, one was discharged and died four months later with severe left ventricular failure.

Discussion

Shock associated with acute myocardial infarction represents severe impairment of ventricular performance and myocardial energy production. The controversy during the past years over the efficacy of various pharmacologic agents resulted in part from an overemphasis on the function of the heart with little consideration given to the factors governing the survival of ischemic myocardium. We have previously demonstrated that potent inotropic stimulation improved myocardial performance but deteriorated myocardial metabolism in patients in shock associated with acute myocardial infarction. Dopamine is a frequently used vasoactive agent in this patient category. Little information, however, is available about its effect on myocardial oxygenation in severe acute ischemic heart disease.

The hemodynamic effects of dopamine depend upon the dose administered and the condition of the patient. In our patients, the dose of dopamine necessary to improve arterial blood pressure and urine flow, also increased heart rate and contractility, two important determinants of myocardial oxygen consumption. The chronotropic and inotropic properties of dopamine are well known and reported in previous studies. Heart rate ranged between 100 and 140 beats/min when dopamine was infused at an average rate of 23 μg/kg/min to hypotensive patients following cardiac surgery. In a very similar patient group, dopamine (5–10 μg/kg/min) raised heart rate from an average of 89 to 111 beats/min, four of the patients exhibiting a heart rate above 120 beats/min. Ten patients in shock associated with acute myocardial infarction showed a progressive increase in heart rate with increasing doses of dopamine; 7.5 μg/kg/min increased heart rate from an average of 107 to 133 beats/min. Higher doses of dopamine caused tachyarrhythmias. Less marked but substantial increases in heart rate following dopamine administration are reported in the literature.

Evaluation of myocardial contractility during the administration of dopamine in the intact organism is complicated by concurrent changes in heart rate, afterload, and preload. Substantial increases in cardiac output and systolic ejection rate in our patient group with only moderate decreases in systemic vascular resistance strongly suggest that dopamine increased myocardial contractility. The positive inotropic properties of dopamine were observed experimentally in normal and ischemic myocardium. Thompson et al. reported the optimal inotropic effect of dopamine in man to be between 5 and 30 μg/kg/min as indicated by increase in cardiac output, pulse pressure and by modest changes in mean arterial pressure and systemic vascular resistance. Increase in contractility by dopamine in man was also shown by significant shortening of the systolic pre-ejection period.

The efficacy of any therapeutic intervention in shock associated with acute myocardial infarction depends upon its balance between myocardial oxygen requirement and supply. Dopamine in our patient group improved ventricular performance at the expense of myocardial oxygenation. Myocardial oxygen extraction, abnormally high prior to treatment, further increased during dopamine infusion evidencing increased oxygen demand and inadequate increase in oxygen supply. The increased rate of myocardial lactate production indicates enhancement of anaerobic metabolism and is additional evidence of the inadequacy of myocardial oxygen supply in relationship to oxygen demand. Myocardial free fatty acid extraction ratios, low prior to dopamine infusion, decreased in four patients suggesting increased ischemia.

Although dopamine is a widely used therapeutic agent in myocardial infarction shock, little is known about its effect on oxygenation of acutely ischemic myocardium. Crexells et al. infused 10 μg/kg/min dopamine to patients with more than 75% obstruction of one or more of the major coronary arteries and found no significant changes in myocardial metabolism. Myocardial lactate extraction ratios averaged 10% and 11% prior to and during dopamine infusion. The trend of changes indicated a decrease in coronary sinus oxygen tension. These results should be considered with caution since they were based on sampling of mixed coronary sinus blood in patients with less ischemic myocardium than our patients had. Venous effluent from the stressed but normal myocardium of Crexells’ patients may have overshadowed the effluent from the ischemic areas, thus masking abnormalities in myocardial metabolism. Forrester et al. studying the awake dog, found that infusion of 5–10 μg/kg/min dopamine after coronary occlusion consistently deteriorated myocardial metabolism. The rate of myocardial lactate production increased from an average of 69 to 92%. Other investigators observed an increase in infarct size and of ischemic injury by dopamine in experimental myocardial infarction, using the open chest dog preparation.

The clinical experience with dopamine in myocardial infarction shock has been variable. A number of investigators demonstrated improvement in cardiovascular and renal hemodynamics during dopamine administration. A significant number of patients survived the shock state but only a few lived very long. Among 24 patients in cardiogenic shock treated with dopamine, ten had an acute myocardial infarction. Three of these ten patients survived the shock episode, but died within one month. Five of our patients received dopamine until intra-aortic counterpulsation was initiated. In the remaining three patients, dopamine temporarily improved the shock state. Two succumbed in the hospital, one was discharged and died four months later due to severe left ventricular failure. These results emphasize the experience of the past decade that although shock in myocardial infarction can be improved by inotropic agents or cardiac assistance, long-term survival
requires improvement of coronary perfusion by aorto-
coronary bypass surgery.

Our observations indicate that dopamine in the doses re-
quired to increase arterial pressure and cardiac output exerts
inotropic and chronotropic effects which are detrimental to
acutely ischemic myocardium. Since improvement of
peripheral circulation is worthless in the face of a deter-
iorating pump, dopamine should be used with caution in pa-
ients in shock associated with acute myocardial infarction.

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