Vasodilator Therapy in Acute Myocardial Infarction

A Comparison of Sodium Nitroprusside and Nitroglycerin

By Paul W. Armstrong, M.D., David C. Walker, M.D., Jeffrey R. Burton, M.D., and John O. Parker, M.D.

SUMMARY

Twenty-six patients with complicated acute myocardial infarction were studied in order to compare the hemodynamic effects of sodium nitroprusside (NP) and nitroglycerin (GTN). All patients received NP and 18 of the 26 also received GTN to evaluate both drugs in the same individuals. Both agents produced significant declines in mean arterial pressure, total peripheral resistance (TPR), and heart rate systolic blood pressure product. However, in the 18 patients who received both drugs GTN produced a greater fall (P < 0.05) in pulmonary capillary wedge pressure (PCW) (25 to 15 mm Hg) than did NP (24 to 17 mm Hg) and a greater increment (P < 0.01) in TPR (0.98 to 1.43) than NP (0.98 to 1.16). These data confirm the potent vasodilatory effects of NP and GTN and suggest that NP has a relatively balanced effect on the arterial and venous circulation, and GTN seems to produce more potent venodilatation than arterial dilatation. These observations provide a basis for a more rational choice of vasodilator agents based on initial hemodynamic measurements in complicated acute myocardial infarction.

Vasodilator Therapy in acute myocardial infarction has been the subject of a number of recent clinical investigations. Such therapy has been utilized in an attempt to favorably alter the hemodynamic profile of patients with acute myocardial infarction so as to reduce myocardial oxygen consumption and improve cardiac performance. Since it is now believed from experimental and clinical studies that acute myocardial infarction is a dynamic process unfolding over many hours, it can be argued that reduction of oxygen consumption in such circumstances may preserve ischemic myocardium that otherwise might progress to necrosis.

Pharmacological agents employed during such therapy have included phenolamine, sodium nitroprusside, and nitroglycerin. Although the hemodynamic effects of these agents have been studied there is no comparative information available concerning their actions. Accordingly, we undertook a hemodynamic study of sodium nitroprusside and nitroglycerin in a group of patients with acute myocardial infarction complicated by hypertension and/or heart failure.

Methods

Twenty-six patients were studied in the first 24 hours after acute myocardial infarction in the Connell Coronary Care Unit of the Kingston General Hospital. Twenty-four of the patients were male and two were female and the average age in the study group was 55 years with a range of 38–76 years. All patients had acute myocardial infarction confirmed by serial electrocardiographic and enzyme determinations. The site of the infarction was anterior in 16, inferior in nine, and subendocardial in one. Peak serum glutamic oxaloacetic transaminase levels were less than 250 mIU/ml in six, between 250 and 500 mIU/ml in nine, and greater than 500 mIU/ml in 11 patients (normal range 10–50 mIU/ml). The patients were grouped according to the Killip classification of acute myocardial infarction: five patients were in group 1, 13 in group 2 and eight in group 3.

The hemodynamic criteria for admission to this study were the presence of hypertension as defined by a mean arterial pressure of greater than or equal to 105 mm Hg and/or a pulmonary capillary wedge pressure greater than 15 mm Hg.

All patients received sodium nitroprusside. Eighteen of the 26 patients also received nitroglycerin in an effort to evaluate both drugs in the same individuals. Nitroprusside was prepared in the hospital pharmacy by a method previously described by Cacace and Thomas and the resulting solution was passed through a Millipore filter into sterile 10 ml vials. This solution was added to a 5% dextrose in water solution just prior to use so as to provide a concentration of 100 µg/ml. It was kept refrigerated and shielded from light and was used within 48 hours of preparation. Nitroglycerin solution was prepared using tablet triturates dissolved in 50 ml of 5% dextrose in water and centrifuged for 10–15 minutes. After the talc-containing supernatant was drawn off the remaining solution was passed through a Millipore filter and into a solution of 5%
vascular resistance was obtained by injecting 10 ml of ice cold 5% dextrose in water into the right atrium. Pressures and outputs were displayed on a VR 6 Electronics-for-Medicine recorder and output curves were computed electronically by an Edwards cardiac output computer. No patient received cardiotonic agents during the study period but five were receiving lidocaine infusion at a constant rate. Observations were made during a control period of 15–20 minutes during which the cardiac output was determined at least in duplicate. Following this, vasodilator therapy was commenced via the intravenous route with the rate controlled by a Harvard infusion pump. The aim of therapy was to normalize blood pressure and/or pulmonary capillary wedge pressure. Once this had been achieved and a steady state maintained for at least 15 minutes, repeat hemodynamic measurements were obtained. The average infusion rate of sodium nitroprusside for the overall group was 76 μg/min; the 18 patients who received both agents had an average infusion rate of nitroprusside of 79 μg/min and an average infusion rate of nitroglycerin of 63 μg/min. The order in which the vasodilator agents were given to the 18 patients who received both drugs was varied.

Derived calculations were performed using the following definitions:

\[ SV = CO \times TPR = MAP - CO = HR \times SBP, ART_d - PCW, TPR, \]

where \( SV \) = stroke volume in ml/beat, \( CO \) = cardiac output in L/min, \( HR \) = heart rate in beats/min, \( TPR = \) total peripheral resistance in units, \( MAP = \) mean arterial pressure in mm Hg, \( HR \times SBP = \) heart rate \times systolic blood pressure in mm Hg/min × 10\(^{-4}\), \( ART_d = \) PCW = transmyocardial gradient in mm Hg obtained by subtracting the pulmonary capillary wedge pressure from the arterial diastolic pressure, \( TPR = \) the ratio of total peripheral PCW resistance over mean capillary wedge pressure. Statistical analysis was performed using Student's t-test with paired and unpaired comparisons where appropriate.

**Results**

Individual hemodynamic data for systolic, diastolic, and mean arterial pressure as well as pulmonary capillary wedge pressure are presented in table 1 and a summary of all hemodynamic data is shown in table 2. The overall group of 26 patients who received nitroprusside showed no change in heart rate but a fall in MAP from 114 to 95 mm Hg, and in PCW from 23 to 16 mm Hg. No change was seen in either cardiac index or SV. TPR fell from 23 to 18 units, and HR \( \times \) SBP likewise fell from 1199 to 1041 mm Hg/min ×

### Table 1

**Individual Hemodynamic Data**

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<th>MAP (mm Hg)</th>
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Abbreviations: SBP = systolic blood pressure; DBP = diastolic blood pressure; PCW = pulmonary capillary wedge pressure; CI = control for nitroprusside; NP = nitroprusside; C1 = control for nitroglycerin; GTN = nitroglycerin.

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10⁻¹. ARTᵩ – PCW fell from 65 to 60 mm Hg and TPR/PCW rose from 1.08 to 1.41.

In the 18 patients who received nitroglycerin there was a fall in MAP from 112 to 97 mm Hg and a reduction in PCW from 25 to 15 mm Hg. This was achieved without any change in cardiac index, HR or SV. TPR fell from 22 to 19 units and HR × SBP fell from 1208 to 1060 mm Hg/min × 10⁻¹. There was no change in ARTᵩ – PCW and the TPR/PCW rose from 0.98 to 1.43.

Comparison of the 18 patients who received both nitroprusside and nitroglycerin revealed that there was no difference in the response of HR or MAP. Despite this, the fall in PCW from 25 to 15 mm Hg with nitroglycerin was significantly greater than the fall from 24 to 17 mm Hg with nitroprusside. Neither drug produced a significant change in cardiac index or SV and both produced similar falls in TPR and HR × SBP. Although the fall from control produced by nitroprusside in the ARTᵩ – PCW (62 to 57 mm Hg) was significant, the fall with nitroglycerin (63 to 62 mm Hg) was not. However, there was no statistical difference between these changes. Comparison of TPR/PCW showed that there was a significantly smaller increment (from 0.98 to 1.16) with nitroprusside than with nitroglycerin which increased from 0.98 to 1.43. These changes are illustrated in figure 1.

![Figure 1](http://circ.ahajournals.org/) This figure plots the ratio of total peripheral resistance divided by pulmonary capillary wedge pressure (TPR/PCW). The plotted points represent the mean values for the 18 patients who received both sodium nitroprusside (NP) and nitroglycerin (GTN). The changes from control produced by nitroglycerin were significantly greater (P < 0.01) than the changes from control with nitroprusside.
Analysis of the response of cardiac index to vasodilator therapy was performed focusing on those patients with PCW greater than or equal to 15 mm Hg after therapy. There were 15 patients in this category who received nitroprusside and no significant change was seen in cardiac index. Although the eight patients in this category who received nitroglycerin had a small increase in cardiac index from 2.6 to 2.8 L/min/m² (P < 0.02), this change is probably of little or no physiological significance.

A representative individual response to vasodilator therapy with both agents is illustrated in figure 2.

Two patients in the study group developed symptomatic hypotension; one with nitroglycerin and the other with nitroprusside infusion. Both episodes were quickly reversed by elevation of the legs and cessation of the infusion. Two patients also developed nausea and vomiting with nitroprusside infusion which was transient and did not necessitate termination of the infusion. Major symptomatic benefit in response to both vasodilator agents was observed in seven patients whose wedge pressures were greater than 25 mm Hg; this consisted of relief of restlessness, diaphoresis, dyspnea, and chest discomfort which was noted to return promptly following cessation of vasodilator infusion.

Discussion

These data indicate that both nitroprusside and nitroglycerin are capable of producing significant improvement in cardiac performance in the setting of complicated acute myocardial infarction. This is demonstrated by the ability of these agents to produce a significant fall in left ventricular filling pressure without a concomitant drop in stroke volume or cardiac index. Furthermore, this improvement in cardiac performance is achieved in the face of a favorable alteration in the determinants of myocardial oxygen consumption. This alteration is achieved in part by the reduction in left ventricular filling pressure or preload which would thereby produce a fall in ventricular volume and wall tension. Additionally, the resistance to left ventricular ejection or afterload is reduced by means of a lowering of systemic arterial pressure unaccompanied by a fall in cardiac index. Furthermore, these effects are achieved without a reflex tachycardia.

There was, however, an important difference in the hemodynamic response of the 18 patients who received both drugs. Nitroglycerin lowered left ventricular filling pressure more substantially than did sodium nitroprusside and it did so despite the fact that both drugs produced similar changes in arterial blood pressure. This response is perhaps best demonstrated by considering the changes in the ratio of total peripheral resistance to left ventricular filling pressure displayed in figure 1. Since both numerator and denominator of this ratio declined with the two agents, the changes displayed indicated a significantly greater fall in preload relative to systemic arterial resistance for nitroglycerin as compared to nitroprusside. This observation confirms that the effect of nitroglycerin on venous pooling is more potent than its effect on arteriolar resistance. Thus, in the 18 patients who received both agents, nitroprusside produced a more balanced change in preload and arteriolar resistance.

Apart from the factors which determine myocardial oxygen consumption, the other key hemodynamic consideration in the management of such patients is the level of coronary perfusion pressure. Since this is a function of transmyocardial gradient, the pressure difference between diastolic arterial and pulmonary capillary wedge pressure was examined during infusion of nitroprusside and nitroglycerin. Virtually no change in the transmyocardial gradient occurred with nitroglycerin whereas a small decrease occurred with nitroprusside.

Figure 2

This figure displays individual data of HR (heart rate), MAP (mean arterial pressure), PCW (pulmonary capillary wedge pressure), and CI (cardiac index) from a representative patient. These data are plotted for C₁ (initial control period), NP (during nitroprusside infusion), C₂ (a second control period), and GTN (during nitroglycerin infusion).
The effects of nitroprusside in acute myocardial infarction have been studied by others with results similar to ours.\textsuperscript{1, 2} Although there were individual instances in which cardiac index rose following infusion of nitroprusside, the response was variable and analysis of the over-all group revealed no significant change. A breakdown of the group on the basis of elevated or normal left ventricular filling pressure failed to better discriminate the response of cardiac index.

There remains some controversy about the effects of nitroglycerin in the setting of acute myocardial infarction. This may be based in part on the route of the delivery since there is presumably a bolus effect following sublingual administration. This has been variously reported to produce a deterioration or an improvement in cardiac performance.\textsuperscript{12, 13} The only other study utilizing the intravenous route for nitroglycerin administration demonstrated similar changes in left ventricular filling pressure and mean arterial pressure as in our own study and no change in heart rate or cardiac index.\textsuperscript{4} These authors employed precordial mapping in some of their patients and found a favorable influence on the height of the injury current. In addition to the peripheral mechanisms already discussed, it is possible that nitroglycerin may produce some changes in ventricular compliance or in the distribution of coronary blood flow in this setting.

The importance of the current study is the opportunity to observe the response of two different vasodilator agents in the same patients. From the data accumulated it is possible to offer some guidelines about the use of these agents in complicated acute myocardial infarction. In a patient with an elevated arterial pressure who has a normal or reduced pulmonary capillary wedge pressure, nitroprusside would appear to be a more reasonable choice because of its more balanced effect on the arterial and venous bed. If, on the other hand, significant elevation of left ventricular filling pressure is present, nitroglycerin would appear to be the most effective agent. It is important to emphasize that in most patients invasive hemodynamic measurements including left ventricular filling pressure and cardiac output are required to adequately monitor this form of therapy. Further studies involving a direct measurement of myocardial oxygen consumption and myocardial infarction size are required to establish the ultimate role of this therapy.

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