Sodium Nitroprusside Therapy for Cardiac Failure in Anesthetized Patients with Valvular Insufficiency

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Cardiac function was evaluated in 17 patients with cardiac valvular insufficiency scheduled for valve replacement 1) immediately prior to the induction of anesthesia, 2) during stable anesthetic and surgical conditions after the chest was opened, and 3) during a constant sodium nitroprusside infusion about 15 min later but prior to cannulation for cardiopulmonary bypass. Preoperative awake hemodynamic measurements indicated that these patients were in a state of compensatory cardiac failure with a low cardiac index of $2.20 \pm 0.15$ l/min/m² and a high systemic vascular resistance of $1,560 \pm 150$ dyne·sec·cm⁻². Pulmonary capillary wedge pressure was $13 \pm 3$ torr, central venous pressure $4 \pm 1$ torr, and stroke volume index was $29.6 \pm 2.1$ ml/beat/m². During steady-state anesthesia with the operation in progress, there were significant increases in systemic vascular resistance to $2,370 \pm 160$ dyne·sec·cm⁻² and pulmonary capillary wedge pressure to $24 \pm 2$ torr, and significant decreases in cardiac index to $1.63 \pm 0.08$ l/min/m² and stroke volume index to $19.4 \pm 1.3$ ml/beat/m², demonstrating cardiac decompensation.

At this time, an infusion of sodium nitroprusside, $20–96$ μg/min, produced significant decreases in systemic vascular resistance to $1,490 \pm 130$ dyne·sec·cm⁻² and pulmonary capillary wedge pressure to $16 \pm 2$ torr. Cardiac index increased to $2.21 \pm 0.15$ l/min/m² and stroke volume index to $24.4 \pm 1.9$ ml/beat/m². These results indicate that patients in compensated cardiac failure secondary to valvular insufficiency respond to anesthesia and operation with a marked deterioration in cardiac function primarily due to a further increase of the already high systemic vascular resistance. Sodium nitroprusside, by decreasing vascular tone and thus ventricular afterload, reverses some of the cardiovascular depression and failure in these patients, thereby mitigating the deleterious effects of anesthesia and operation. (Key words: Anesthesia, cardiovascular. Heart: cardiac output; failure; myocardial function; vascular pressures. Anesthetic techniques, hypotension, induced, nitroprusside.)

Sodium nitroprusside is a potent vasodilating agent that has a direct action on peripheral vascular smooth muscle independent of autonomic control.1 Given as an intravenous infusion it has a rapid onset and a short duration of action. These properties allow easy control of vascular resistance, and thus its application to clinical situations is expanding. Patients with refractory heart failure secondary to ischemic heart disease, cardiomyopathies, or valvular insufficiency have all shown significant hemodynamic and clinical improvement during sodium nitroprusside therapy in intensive care units.2–4 In such patients the drug produced a marked decrease in ventricular outflow impedance which, in turn, caused an increase in cardiac output and a decrease in ventricular filling pressures. Nitroprusside is particularly useful in patients with valvular insufficiency because it decreases the regurgitant fraction, augments the forward output of the heart, and thus promotes efficiency and better overall cardiac function.2–7

During anesthesia and operation for myocardial revascularization, sodium nitroprusside has been shown to enhance cardiac performance in patients with either acute or chronic left ventricular dysfunction.8 There is also a case report in which nitroprusside was essential in weaning a patient from cardiopulmonary bypass following mitral valve replacement.9 However, nitroprusside has not yet been advocated for use in anesthetized patients with cardiac failure secondary to valvular insufficiency in the critical period prior to cardiopulmonary bypass and surgical correction. We have observed that these patients often experience an abnormally high systemic vascular resistance, an extremely low cardiac output, and pulmonary congestion in response to light anesthesia and surgical stimulation, and we believed that patients in this situation would benefit from sodium nitroprusside therapy as part of their pre-bypass anesthetic management.

The purpose of this study, therefore, was to document the cardiovascular deterioration produced by anesthesia and operation in this compromised population and then to evaluate the therapeutic effectiveness of sodium nitroprusside in reversing the exacerbated cardiac failure.

Methods

Seventeen patients, all of whom had histories of chronic congestive heart failure and vigorous treatment with digitalis and diuretic agents, were scheduled for correction of their valvular insufficiency after cardiac catheterization. Nine patients had predominant mitral valvular regurgitation, six had predominant aortic valvular regurgitation, and in two others both valves were incompetent. No patient had sig-

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significant mitral or aortic stenosis. Atrial fibrillation was present in ten patients, while the remaining seven manifested a sinus rhythm. There were 11 female and six male patients, ranging in age from 36 to 77 years, and all were classified ASA physical status III or IV.

All patients were premedicated by intramuscular injection of morphine, 3–10 mg, and scopolamine, 0.2–0.5 mg, 90 min prior to induction of anesthesia. A seven-lead EKG was continuously monitored, and a 20-gauge cannula was inserted into a radial artery for direct arterial pressure measurement. A triple-lumen, balloon-tipped, thermodilution Swan-Ganz catheter was introduced through the right internal jugular vein and was flow-directed into the wedge position in a pulmonary artery under continuous EKG and pressure monitoring. Pressures were measured with Statham P23 ID transducers, displayed on an oscilloscope and recorded on a Hewlett-Packard eight-channel thermal tip chart recorder. Multiple determinations of cardiac output were obtained by the thermodilution technique using an Edwards Laboratory Thermodilution Cardiac Output Computer (model 9510-A).

Precordiastolic measurements included: heart rate, (HR), systemic arterial pressure (SAP), central venous pressure (CVP), pulmonary arterial pressure (PAP), pulmonary capillary wedge pressure (PCWP) and cardiac output (CO). Standard formulas were used to derive cardiac index (CI), stroke volume index (SVI), systemic vascular resistance (SVR), and pulmonary vascular resistance (PVR).

Anesthesia was induced with morphine, 0.5–1 mg/kg, in divided doses while the patient was breathing 100% oxygen by mask. Intubation of the trachea was attempted when the lid reflex was lost and was facilitated with succinylcholine, 1 mg/kg, after pretreatment with d-tubocurarine, 3 mg. Anesthesia was maintained with morphine (total dose 1–2 mg/kg) and nitrous oxide 0–60% per cent. Although it was realized that nitrous oxide increases systemic vascular resistance, its anesthetic properties were necessary in some of the patients, and its concentration was always kept constant throughout a given study. Muscle relaxation was maintained with d-tubocurarine, 0.5–1 mg/kg. Ventilation was controlled, and arterial carbon dioxide partial pressure kept between 30 and 40 torr.

After the chest and pericardium were opened through a medium sternotomy and a steady hemodynamic state was established (i.e., stable HR, SAP, CVP and PWCP for about 10 min), a second complete set of measurements as described previously was obtained. Sodium nitroprusside was then infused at a rate in the range of 20–96 μg/min. The infusion was begun slowly and then gradually the rate was increased and titrated to achieve the maximum decrease in PCWP while maintaining SAP near preinduction levels. After the above-mentioned conditions had been satisfied for 10–15 min, a third set of measurements was obtained. Surgical dissection had advanced at this point, but it was not thought that surgical manipulation compromised the hemodynamic status of any patient, and it is hardly likely that it caused any cardiovascular improvement. All measured values were recorded before cannulation for cardiopulmonary bypass, at which time the nitroprusside infusion was stopped. No vasopressor drug was used immediately prior to or during nitroprusside infusion. Total fluid administration preceding cardiopulmonary bypass ranged from 200 to 300 ml of dextrose, 5 per cent, in lactated Ringer's solution, and the infusion rate was not increased during nitroprusside administration. Estimated blood loss prior to cannulation did not exceed 200 ml in any patient, and hypotension associated with cardiac cannulation was unusual and minimal when it occurred. Body temperature, measured with an esophageal thermistor, decreased no more than 3°C over the period between induction of anesthesia and onset of cardiopulmonary bypass. Data were analyzed by t test for paired data. P < 0.05 was considered significant.

Results

From preinduction data (table 1), it can be seen that these patients came to the operating room in compensated cardiac failure following a vigorous medical regimen of digitalis and diuretic agents. Although blood pressure and heart rate were within normal limits, the mean preinduction cardiac index was only 2.20 ± 0.15 l/min/m², and SVR was abnormally increased at 1,560 ± 150 dynes·sec·cm⁻². PCWP was 13 ± 3 torr and CVP 4 ± 1 torr, both surprisingly low considering that these patients had sufficient valvular regurgitation and cardiac failure to warrant valve replacement.

Adoministration of anesthesia and surgical stimulation caused a decompensation in the hemodynamic state of these patients (table 1). SAP increased from 72 ± 3 to 89 ± 4 torr, while systemic vascular resistance and pulmonary vascular resistance increased far beyond their already high preoperative values. There was a 34% decrease in stroke volume index from 29.6 ± 2.1 to 19.4 ± 1.3 ml/beat/m². Although heart rate increased from 77 ± 4 to 88 ± 4 beats/min, cardiac index decreased 26 per cent, from 2.20 ± 0.15 to 1.63 ± 0.08 l/min/m², concomitantly, with increases in ventricular filling pressures (PCWP, 13 ± 3 to 24 ± 2 torr and CVP, 4 ± 1 to 8 ± 1 torr). Thus,
cardiac performance deteriorated and failure became severe.

The sodium nitroprusside infusion tended to ameliorate this decompensated hemodynamic state (table 1). Marked decreases in SVR (2,370 ± 160 to 1,490 ± 130 dynes·sec·cm⁻²) and PVR (270 ± 64 to 153 ± 27 dynes·sec·cm⁻²) occurred and were accompanied by a return to preinduction levels of SAP and PAP. In addition, the decrease in vascular resistance was associated with a 36 per cent increase in cardiac index from 1.63 ± 0.08 to 2.21 ± 0.15 l/min/m². Although heart rate increased 7 beats/min, stroke volume index was also significantly increased by nitroprusside (19.4 ± 1.3 to 24.4 ± 1.9 ml/beat/m²). Moreover, PCWP and CVP decreased to almost normal values (24 ± 2 to 16 ± 2 torr and 8 ± 1 to 6 ± 1 torr). Thus, the administration of sodium nitroprusside produced a marked improvement in the hemodynamic status of anesthetized patients prior to cardiopulmonary bypass and surgical correction of their valvular insufficiency.

**Discussion**

Chronic congestive heart failure, secondary to valvular insufficiency, is characterized not only by a diminished cardiac output but also by increased systemic vascular resistance. This increased vascular tone, which has been attributed to both reflex activation of sympathetic nervous discharge and exaggerated renin–angiotensin release, explains the frequently observed normal blood pressure of patients who have compensated cardiac failure. However, this compensatory state is not altogether beneficial, for it results in an increased impedance to left ventricular ejection. Although normal hearts may tolerate a high outflow impedance without a diminution of stroke volume, failing hearts, when faced with the same increased afterload, manifest a decrease in stroke volume, and cardiac dysfunction becomes even more pronounced.

In this patient population, the combined stress of anesthesia and operation further increased the already higher-than-normal systemic and pulmonary vascular resistances seen in the preinduction period and thus exacerbated the pre-existent compromised hemodynamic state (fig. 1). For a failing ventricle to maintain the same cardiac output against a marked increase in vascular tone, a higher systolic wall tension must be generated. As the diseased heart may already be working at its maximum, it may not be able to meet the newly imposed demands. During anesthesia the usual signs and symptoms of congestive heart failure are not always apparent, and we did not elicit rales, a third heart sound, or other clinical manifestations. Nevertheless, cardiac output decreased and ventricular filling pressures increased, indicating that cardiac failure had become more profound.

To offset the deleterious effects of anesthesia and operation in these patients, sodium nitroprusside was administered intraoperatively. Nitroprusside, by lowering systemic and pulmonary vascular resistances, caused a decrease in ventricular afterload, which, in turn, produced significant increases in both cardiac and stroke volume indices (fig. 1). Ventricular emptying was thus enhanced, and a secondary decrease in ventricular end-diastolic pressure undoubtedly followed.

Sodium nitroprusside, however, acts also upon the venous capacitance vessels to cause venodilatation and venous pooling. Venous return therefore decreases and ventricular filling pressures are also

<table>
<thead>
<tr>
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<th>(1) Preinduction</th>
<th>(2) Anesthesia and Operation</th>
<th>(3) Nitroprusside Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systemic arterial pressure (torr)</strong></td>
<td>72 ± 3</td>
<td>89 ± 4*</td>
<td>72 ± 2*</td>
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<tr>
<td><strong>Central venous pressure (torr)</strong></td>
<td>4 ± 1</td>
<td>8 ± 1*</td>
<td>6 ± 1</td>
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<tr>
<td><strong>Pulmonary arterial pressure (torr)</strong></td>
<td>24 ± 4</td>
<td>34 ± 4</td>
<td>22 ± 3*</td>
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<tr>
<td><strong>Pulmonary capillary wedge pressure (torr)</strong></td>
<td>13 ± 3</td>
<td>24 ± 2</td>
<td>16 ± 2*</td>
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<tr>
<td><strong>Heart rate (beats/min)</strong></td>
<td>77 ± 4</td>
<td>88 ± 4</td>
<td>95 ± 5</td>
</tr>
<tr>
<td><strong>Stroke volume index (ml/beat/m²)</strong></td>
<td>29.6 ± 2.1</td>
<td>19.4 ± 1.3*</td>
<td>24.4 ± 1.9*</td>
</tr>
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<td><strong>Cardiac index (l/min/m²)</strong></td>
<td>2.20 ± 0.15</td>
<td>1.65 ± 0.08*</td>
<td>2.21 ± 0.15*</td>
</tr>
<tr>
<td><strong>Systemic vascular resistance (dynes·sec·cm⁻²)</strong></td>
<td>1,560 ± 150</td>
<td>2,370 ± 160*</td>
<td>1,490 ± 130*</td>
</tr>
<tr>
<td><strong>Pulmonary vascular resistance (dynes·sec·cm⁻²)</strong></td>
<td>170 ± 36</td>
<td>270 ± 64</td>
<td>153 ± 27</td>
</tr>
</tbody>
</table>

Values are mean ± SE. Statistical analysis by Student's t test for paired data. All changes from (1) to (2) and from (2) to (3) achieved a probability of at least P < 0.05; those marked * achieved a probability of P < 0.001.
decreased. One might then tend to attribute the improvement in cardiac performance seen in patients with congestive heart failure during nitroprusside infusion to that property of the drug that decreases preload by venodilatation. However, Cohn et al. have demonstrated that patients with acute heart failure responded to phlebotomy or the application of rotating tourniquets with a diminution of stroke volume, whereas the same patients experienced an increased stroke volume when an equal decrease in left ventricular filling pressure was achieved with an infusion of sodium nitroprusside.\(^29\) Nitroprusside, therefore, decreases preload by two distinctly different mechanisms, but cardiac performance is improved by only that mechanism that diminishes afterload and thus permits greater ventricular emptying. Preload then decreases, but as a result of improved cardiac function and not as the cause of it.

The Frank-Starling law of the heart states that when resting cardiac muscle is stretched, the heart contracts with increased force. Patients in cardiac failure despite maximal inotropic support ought then to respond best to a combination of a decrease in afterload and an increase in preload.\(^21\) In fact, it may be counterproductive in patients with heart failure to permit preload to decrease to a level that is proper for nonfailing hearts. In the immediate postoperative period, Sisson et al. found that sodium nitroprusside was even more effective in increasing stroke volume in patients with cardiac dysfunction following myocardial revascularization when the left atrial pressure was restored to its prenitroprusside infusion level of 15 torr by the transfusion of whole blood.\(^22\)

In the present report, fluids were not administered in large quantities during the nitroprusside infusion because the PCWP decreased to only 16 torr, a level usually deemed appropriate for patients with cardiac failure.\(^23\) However, in these patients sodium nitroprusside produced an increase in heart rate and a decrease in mean arterial pressure, while others have reported that sodium nitroprusside is most effective in the treatment of cardiac failure when these hemodynamic variables do not change with the infusion.\(^6,24\) Perhaps the PCWP of 16 torr, recorded during nitroprusside administration, did not indicate an adequate circulating blood volume but reflected the high systemic vascular resistance (1,400 dynes·sec·cm\(^{-5}\)) coupled with a decreased circulating blood volume. The patients described here did receive sodium nitroprusside during the rigors of anesthesia and operation, when the circulating levels of catecholamines are presumably high.\(^25\) Certainly these two factors together would be sufficient to explain the PCWP of 16 torr, as well as the increase in heart rate and decrease in arterial pressure that occurred during the administration of nitroprusside. Corroborative evidence of the relative hypovolemic status of these patients can be found in their preoperative measured values, as these individuals, with histories of chronic cardiac failure, were brought to the operating room with normal or near-normal central venous and pulmonary capillary wedge pressures. Although blood volume was not measured in this study, it is tempting to speculate that even though vigorous preoperative diuretic therapy makes patients less dyspneic and more comfortable, it does so at the cost of a contracted blood volume.\(^24\) We believe that these “normal” filling pressures cannot represent adequate cardiac function and must therefore indicate the aforementioned composite hemodynamic situation of increased systemic vascular resistance and decreased intravascular volume. Such patients are, in fact, in a very tenuous hemodynamic state, as revealed by the deterioration of their condition in response to the stress of anesthesia and operation. Perhaps had the intravascular volume been increased significantly prior to or during the nitroprusside therapy, heart rate and arterial pressure would have remained unchanged and the

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**FIG. 1. Hemodynamic profile during the preinduction period, anesthesia and operation, and the infusion of sodium nitroprusside. Vertical bars represent SEM, n = 17.**

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**SYSTEMIC VASCULAR RESISTANCE (dynes·sec·cm\(^{-5}\))**

- Pre-induction: 2500
- Nitroprusside: 2000, 1500

**PULMONARY WEDGE PRESSURE (torr)**

- Pre-induction: 24
- Nitroprusside: 18, 12

**STROKE VOLUME INDEX (ml/beat/m\(^2\))**

- Pre-induction: 30
- Nitroprusside: 25, 20

**CARDIAC INDEX (L/min/m\(^2\))**

- Pre-induction: 2.4
- Nitroprusside: 2.0, 1.6
improvement in stroke volume would have been even greater. It may well be more appropriate to titrate the dose of nitroprusside against the systemic vascular resistance, and simultaneously to adjust the preload and SAP by volume expansion as vascular tone is gradually reduced toward normal.

In summary, we found that the ventricular unloading effect of sodium nitroprusside was itself sufficient to produce a general improvement in the hemodynamic performance of anesthetized patients in cardiac failure with heart disease secondary to valvular insufficiency. We saw no undue hypotension in these patients when ventricular filling pressures remained adequate and the therapeutic dosage was gradually approached, and we therefore recommend the use of sodium nitroprusside during anesthesia in patients with valvular insufficiency whenever cardiac failure must be overcome.

References