Nitroprusside after Open-Heart Surgery

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SUMMARY The effects of intravenous infusion of sodium nitroprusside were studied in 11 children immediately after open-heart surgery for congenital heart disease. The patients were selected because, following bypass, their cardiac index was below 2.0 L/min/m² and their systemic vascular resistance exceeded 30 units.

INTRAOPERATIVE MYOCARDIAL DEPRESSION may occur following repair of congenital cardiac defects, especially after procedures that require significant intervals of interruption of coronary flow. The usual response to an inadequate cardiac output secondary to myocardial insufficiency is an increase in systemic vascular resistance.1 Vascular resistance is also frequently increased following the use of hypothermia during perfusion.2

Reduction of systemic vascular resistance by intravenous infusion of sodium nitroprusside has been reported3-7 to improve the hemodynamic status of patients with congestive cardiac failure and with acute myocardial infarction. In response to nitroprusside infusion, Guiha et al.6 observed a prompt decrease in left ventricular filling pressure, an increase in cardiac output, and a fall in systemic vascular resistance in a group of patients with intractable cardiac failure caused by cardiomyopathy or ischemic heart disease. Chatterjee et al.3 noted an improved cardiovascular performance of patients who had an acute myocardial infarction and a left ventricular filling pressure of greater than 15 mm Hg during vasodilator therapy.

Palmer and Lasseter4 suggest sodium nitroprusside is an ideal agent to lower blood pressure because of its rapid onset of action, direct effect to relax vascular smooth muscle, few side effects, relative absence of toxicity in the usual thera-

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Received December 26, 1975; revision accepted April 5, 1976.
The therapeutic dose range (0.5–8.0 μg/kg/min), and rapid reversal of effects on withdrawal. The purpose of this study was to evaluate the response to intravenous infusion of sodium nitroprusside in patients with low cardiac output and increased systemic vascular resistance intraoperatively following cardiopulmonary bypass.

**Materials and Methods**

From a consecutive series of 179 patients undergoing open-heart surgery for congenital heart disease 90 had ventricular function studies. Eleven of the children were selected on the basis of a cardiac index (CI) below 2.0 L/min/m² and a systemic vascular resistance (SVR) of greater than 30 units. These patients ranged in age from one to 12 years and in weight from 5.0 to 29.5 kg. Since the children studied varied widely in weight and surface area, we used the following formula to calculate systemic vascular resistance SVR (in units):

\[ SVR = \frac{MAP - MSVP}{CI} \]

where MAP = mean arterial pressure; MSVP = mean systemic venous pressure in mm Hg; CI = cardiac index in L/min/m². The premedication used in our patients included atropine, ketamine, morphine, pentobarbital, and fentanyl. The agents employed during anesthesia were oxygen, nitrous oxide, morphine, tubocurare or pancuronium. None of our patients who were treated with nitroprusside received inotropic or pressor agents.

After induction of anesthesia and endotracheal intubation a central venous pressure line was inserted and the radial artery cannulated for pressure measurement. The chest was opened by median sternotomy. After isolation of the great vessels, an electromagnetic flow probe was placed around the ascending aorta to determine cardiac output. Systemic vascular resistance was calculated electronically. The aorta and cavae were then cannulated for cardiopulmonary bypass. In nine patients body temperature was lowered by perfusion to 31°C, and the aorta was temporarily occluded for periods of a maximum of 15 min to interrupt coronary blood flow. The duration of hypothermic circulatory arrest in two patients with deep hypothermia (20°C) was 25 and 34 min. After completion of surgical repair of the cardiac defects, body temperature was restored to 37°C and bypass discontinued. The aortic cannula and the superior vena cava catheter were removed and the inferior vena cava catheter was withdrawn to the right atrium for blood transfusion. An electromagnetic flow probe of appropriate size was again placed around the root of the ascending aorta for measurement of cardiac output.

Arterial pressure, cardiac output, and systemic vascular resistance were displayed continuously by digital readout and were recorded. All patients were in sinus rhythm during the studies. A small catheter was inserted in the left atrium for continuous measurement of pressure. While hemostasis was being achieved measurements of the above parameters were observed. Left atrial pressure was serially increased by blood transfusion from the bypass pump via the right atrial catheter until a cardiac index of at least 2.0 L/min/m² was achieved.

In those patients in whom the cardiac index did not exceed 2.0 L/min/m² by increasing left atrial pressure and in whom the SVR was greater than 30 units, sodium nitroprusside (NP) was infused intravenously at rates that ranged from 1.6 to 6.8 μg/kg/min. Left atrial pressure was maintained nearly constant by blood transfusion to approximate post-bypass control levels. We selected the highest left atrial pressures before and after nitroprusside infusion that were nearly equal in order to evaluate the effect of nitroprusside. After a level of left atrial pressure and a rate of infusion of sodium nitroprusside had been established that would maintain a cardiac index of at least 2.0 L/min/m², the flow probe was removed and the patient's chest was closed. The infusion of NP was continued for 3 to 30 hours. The paired Student's t-test was employed for statistical analysis. Each patient served as his own control.

**Results**

Table 1 is a summary of the clinical details of the patients who were infused with sodium nitroprusside, along with the dose and duration of treatment. The values before and after infusion of nitroprusside and percentages of change in arterial pressure, cardiac index, and systemic vascular resistance at a relatively controlled left atrial pressure are recorded in Table 2. When NP was infused and the left atrial pressure was relatively constant, the mean of the percentages of the decreases in arterial pressure was 18.6 ± 7.0, in systemic vascular resistance 53.7 ± 12.5, and the increase in cardiac index 76.9 ± 56.0. There was a significant change (P < 0.01) in arterial pressure, cardiac index, and systemic vascular resistance as a result of NP infusion without a significant change (NS) of left atrial pressure.

Cases 1 and 2, who were subjected to total circulatory arrest at 20°C, had a marked increase in systemic resistance (Table 2). Figure 1 illustrates the changes in left atrial pressure, arterial pressure, cardiac index and SVR in response to NP administration to case 6 after closure of a ventricular septal defect. Blood was transfused from the heart-lung machine to maintain relatively constant left atrial pressure. The marked decrease in SVR from 60 to 24 units was associated with a rise in the cardiac index from 1.7 to 3.0 L/min/m². Simultaneously, mean arterial pressure decreased from 107 to 83 mm Hg.

Because the cardiac index was only 1.4 L/min/m² after

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<th>TABLE 1. Summary of Clinical Data of 11 Patients, Infusion Rate of Sodium Nitroprusside and Duration of Infusion</th>
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**Abbreviations:** Rate = infusion rate of NP (μg/kg/min); NP = nitroprusside; TAPVR = total anomalous pulmonary venous return; VSD = ventricular septal defect; PS = pulmonic stenosis; ASD = atrial septal defect; INF = infundibular; TF = tricuspid atresia; TP = Fallot procedure; TF = coarctation of Fallot; VAL = valvular.
perfusion of case 5, left atrial pressure was successively increased by transfusion while sodium nitroprusside was infused. Figure 2 illustrates the rise in the cardiac index to 2.6 L/min/m² and fall in vascular resistance. Under relatively stable conditions the average hourly urinary output was 81% greater during nitroprusside infusion than in the 3 hour interval after it was discontinued. It is recognized that in this immediate postoperative period many factors would affect
the volume of urinary output such as blood transfusion, intravenous fluids, and level of electrolytes.

Discussion

In 1970 we determined left atrial and arterial pressures, cardiac output, and systemic resistance of 20 selected patients after cardiopulmonary bypass. Four of these 20 patients had a cardiac index below 2.0 L/min/m² and two of these four died postoperatively.

Ventricular function studies were performed on 90 patients of the consecutive series of 179 subjected to cardiopulmonary bypass during the period 1974-75. Systemic vascular resistance exceeded 30 units in a total of 28 of 90 patients who were studied. However the cardiac index was greater than 2.0 L/min/m² in 11 of these patients and no treatment was instituted. Seventeen of these 90 patients had a cardiac index below 2.0 L/min/m². Eleven of these 17 were treated with nitroprusside, and these 11 patients are the basis of this report. Five patients were treated with phentolamine, epinephrine, or isoproterenol to increase cardiac output and survived. The one patient who died postoperatively received no vasodilating or inotropic agent and the mechanism of death was consistent with low cardiac output syndrome.

In the 1974-75 period, 22 of 179 patients died postoperatively (a hospital mortality of 12.4%). Thirteen of these 22 patients who died after surgery included infants who were not studied because their aortic diameter was too small for our flow probes or who had an aortic position that did not readily permit placement of a flow probe. Five of the remaining nine were not studied because of technical reasons. The other four had intra-operative studies and were treated with epinephrine, phentolamine, or isoproterenol for ventricular impairment.

Thus it appears that a cardiac index of below 2.0 L/min/m² after cardiopulmonary bypass is associated with a poor prognosis. This conclusion is supported by the intra-operative studies done by us and by the postoperative studies by Parr et al.13 who reported a mortality rate of 22% when the cardiac index was between 1.5 and 2.0 L/min/m². Furthermore this mortality rose to 40% when the cardiac index was 1.0 to 1.5 L/min/m² and 100% when the index was below 1.0 L/min/m². For these reasons we have hesitated to perform a control study in patients with a low cardiac output.

The cardiovascular actions of sodium nitroprusside have been summarized previously.14,15 Da Luz et al. have shown experimentally that NP significantly enhanced the performance of the heart which had been subjected to acute regional ischemia.16 Guiha et al.4 have emphasized that the improvement in left ventricular output by infusion of NP is due to the reduction of afterload and not due to a change in contractility. However, Miller et al.7 suggest that if there is any minimal increase in contractility associated with the infusion of NP it may be related to a mild increase in sympathetic discharge secondary to the decrease in arterial pressure or a result of decreasing myocardial oxygen consumption.

In some instances, varying intervals of myocardial ischemia are used to facilitate the repair of complex congenital cardiac defects.14 We have previously demonstrated the depressant effects of ischemia on cardiovascular performance experimentally16 and in man.5 Furthermore, certain anesthetic agents may add to the degree of myocardial depression. Hypothermic cardiopulmonary bypass is frequently employed to decrease myocardial oxygen consumption during interruption of coronary blood flow. These maneuvers allow the use of a lower flow rate during total body perfusion and minimize the volume of blood in the operative field. Recently the technique of hypothermic circulatory arrest has been introduced to aid in the repair of cardiac defects in infants. Exposure of the patient to hypothermia is associated with a rise in systemic vascular resistance.5 We have observed a marked decrease in left ventricular output following bypass at 20°C and confirmed the significant increase in systemic resistance.10 We also noted that cardiac performance was improved by lowering the impedance to left ventricular ejection. Thus, it seems prudent to use NP to improve the cardiac output of children after bypass who have depressed contractility, increased systemic vascular resistance, and a low cardiac index.

The study indicates the value of continuous measurement of cardiac output immediately after cardiopulmonary bypass. This facilitates the computation and display of systemic vascular resistance. After bypass, we attempted to increase preload by transfusion of blood until the cardiac index was above 2.0 L/min/m². When the cardiac index was below 2.0 L/min/m² and when the systemic resistance was significantly increased, we infused sodium nitroprusside in a serially increased dose until SVR had decreased and the CI increased to greater than 2.0 L/min/m². We used the value of systemic resistance prior to perfusion as a guide to a suitable postoperative level. At the onset of nitroprusside infusion, blood transfusion was frequently necessary to maintain a nearly constant left atrial pressure (fig. 1). We also observed that discontinuation of infusion of NP may be associated with an increase in left atrial pressure, especially when the infusion was discontinued abruptly.

After an optimal infusion rate of NP and level of left atrial pressure had been established that would maintain a cardiac index above 2.0 L/min/m² the flow probe was removed and the chest was closed. Since the effect of hypothermia on sympathetic vascular tone is of limited duration, NP may be discontinued several hours following bypass if SVR is elevated on the basis of hypothermia only. Similarly, the heart may recover rapidly from ischemia and NP would no longer be necessary.

When left atrial pressure has been increased excessively by transfusion in the presence of a low CI, NP is effective in lowering preload and increasing cardiac output. This is demonstrated in figure 3 which shows data from a 24-year-old female who had mitral insufficiency of rheumatic origin and congestive cardiac failure. (This patient is not included in tables 1 or 2). Immediately after mitral valve replacement, her cardiac index was only 0.6 L/min/m² with a left atrial pressure of 26 cm H₂O and systemic vascular resistance of 70 units. After NP was begun, SVR decreased to 24 units. Since left atrial pressure was unduly lowered to 10 cm H₂O by NP infusion, blood transfusion was necessary to increase preload which resulted in an increase of the cardiac index to 2.5 L/min/m².

Although blood replacement is increased until hemostasis
is achieved, the net quantity of blood necessary to keep the left atrial pressure stable during the onset of nitroprusside infusion ranged from 3 to 5 ml/kg of body weight. When nitroprusside was started left atrial pressure decreased by 7 to 16 cm H₂O from the control level if no blood was transfused.

Vatner and Braunwald have emphasized that general anesthesia and surgical trauma result in significant changes in cardiovascular dynamics and, in addition, may alter greatly the response of the circulatory system to pharmacologic agents. Since it is essential to know the cardiovascular status immediately after bypass, by necessity the hemodynamic measurements of the study were performed under conditions of general anesthesia, positive pressure ventilation with the chest open, and following surgical repair of cardiac defects. In evaluating the control state and the response to NP infusion the above factors must be taken into consideration.

All of our patients were considered to have normal hepatic and renal function. We did not observe any signs of NP toxicity such as trembling, rigidity, or convulsions. We suggest that the infusion rate of NP be limited to 0.5 to 8.0 µg/kg/min. Davies et al. have reported a case in which sudden death occurred as a result of a much larger dose (120 µg/kg/min).

Our data suggest that children are capable of greater changes in vascular resistance in response to NP than those reported in adults. Case 1 was subjected to 34 min of total circulatory arrest at 20°C while the repair of total anomalous pulmonary venous return was performed. A marked increase in systemic vascular resistance was observed along with a very low cardiac index. Although this may be tolerated in many instances, we believe the use of NP which is associated with an increase in cardiac output provides a greater margin of safety for recovery. Parr et al. reported that the mortality rate after bypass is lower when the cardiac index was maintained above 2.0 L/min/m² in infants and young children. This study suggests that rational patient management immediately after bypass is facilitated by knowledge of cardiac index and SVR. In these patients, nitroprusside is effective in lowering systemic vascular resistance and improving cardiac output, especially when left atrial pressure is maintained by blood transfusion.

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Circulation. 1976;54:467-471
doi: 10.1161/01.CIR.54.3.467

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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the World Wide Web at:
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