Hemodynamic Effects of Intravenous Sodium Nitroprusside in the Conscious Dog

Massimo Pagani, M.D., Stephen F. Vatner, M.D., and Eugene Braunwald, M.D.

SUMMARY The hemodynamic effects of 7 min i.v. sodium nitroprusside (NP) were studied in conscious dogs previously instrumented for measurement of arterial pressure, cardiac output, regional blood flow distribution, left ventricular (LV) pressure, and internal dimensions. Nitroprusside, 25 μg/kg/min, reduced mean arterial pressure by 23 ± 3%. Cardiac output increased initially by 39 ± 7% and returned toward control by the end of the infusion. Regional blood flows increased relatively; the relative rise was greatest in the coronary (+225 ± 39%), intermediate in the mesenteric (+98 ± 23%) and iliac (+38 ± 6%), and least in the renal (+10 ± 3%) bed. By the end of the infusion period the vasodilation was unchanged in the renal bed, less intense in the coronary and mesenteric, while in the iliac bed, blood flow was reduced and resistance was actually increased by 33 ± 11% above control. A generalized vasoconstriction ensued after cessation of infusion. In contrast, when the drug was administered intra-arterially to the iliac bed, arterial pressure did not fall and only iliac vasodilation was observed. Peak cardiac effects were characterized by increases in heart rate and LV dP/dt, along with marked reductions in LV end-systolic diameter (~13 ± 2%), and in end-diastolic diameter (~17 ± 2%) and pressure. LV end-diastolic diameter fell even when heart rate was maintained at a constant rate by pacing.

Thus, in the conscious dog, NP reduced LV dimensions substantially, while inducing changes in peripheral beds. The differences in these effects depend on interactions between the direct effects of NP and the opposing effects of reflex adjustments which appear sufficiently powerful to result in net constriction of the iliac bed late during the infusion.

THE INTRAVENOUS ADMINISTRATION OF SODIUM NITROPRUSSIDE (NP) has been shown to be of hemodynamic benefit in patients with acute or chronic left ventricular failure. Its beneficial effects are generally attributed to reductions of left ventricular (LV) afterload, secondary to arterial vasodilation, as well as preload, secondary to venodilation. Additional effects on myocardial relaxation and on LV diastolic properties have also been reported. However, despite its clinical importance, the circulatory actions of NP are still incompletely understood, both in physiological and pathologic situations. Most prior studies of this drug have been limited in that they were conducted in conscious patients where measurements were of necessity made intermittently due to the technical limitations dictated by the use of human subjects, or in anesthetized animal preparations where the complicating effects of anesthesia and recent surgery are present.

The goal of the present study was to characterize more completely the hemodynamic effects of intravenously administered NP in the normal conscious dog. Hemodynamic measurements were obtained instantaneously and continuously before, during, and after the intravenous infusion of this drug in order to study the temporal sequence of the hemodynamic changes. This approach was employed since the reduction in arterial and cardiac pressures induced by the direct relaxant action on vascular smooth muscle might be expected to induce reflex cardiovascular adjustments and the resultant pattern of hemodynamic responses might be complex and vary both in time and intensity as occurs with nitroglycerin.

Methods

Twenty-one mongrel dogs, weighing 20–35 kg, were anesthetized with intravenous pentobarbital, Na, 30 mg/kg. Through a left thoracotomy in the fifth intercostal space, a Doppler ultrasonic or electromagnetic flow transducer* was
implanted around the left circumflex coronary artery. A miniature pressure transducer* was implanted through a stab wound in the LV apex. Ultrasonic dimension transducers were implanted on opposing LV anterior and posterior endocardial surfaces (7 dogs) to measure internal diameter and pacing electrodes were sutured to the left atrium. In six additional dogs, an electromagnetic flow transducer† was implanted around the ascending aorta. Through a midline laparotomy, Doppler ultrasonic or electromagnetic flow transducers‡ were placed around the mesenteric, renal, and iliac arteries (7 dogs). In all dogs, a heparin-filled Tygon catheter was implanted in the thoracic aorta through a lumbar branch or directly in the descending thoracic aorta. A left atrial catheter was implanted in the animals instrumented with LV pressure gauges to calibrate diastolic LV pressure in vivo.

Arterial and left atrial pressures were measured with Statham P23Db strain gauge manometers.‡ LV pressure was measured with the implanted miniature pressure gauge. An improved ultrasonic transit time dimension gauge was used to measure LV diameter; the details of this technique have been published previously.³⁴

Regional blood flow was measured with a Doppler ultrasonic flowmeter, which has been described in detail previously³⁵,³⁶ and has an accurate electronic zero reference or an electromagnetic flowmeter.§ With the latter, zero flow was determined by inflation of an occluding cuff implanted distal to the probe; it was assumed to occur during late diastole, when aortic blood flow was measured.

The data were recorded on a multichannel analog tape recorder and played back on a direct-writing oscillograph. A cardiotachometer, triggered by a signal from the pressure pulse, provided instantaneous and continuous records of heart rate. Electronic resistor-capacitor filters with 2-sec time constants were used to derive mean arterial blood pressure and mean regional and coronary blood flows, and an 8-sec time constant was used to derive mean aortic flow. Mean regional vascular resistance in any bed was calculated as the quotient of mean arterial pressure and regional flow in that bed. Regional resistances could be continuously measured by a simple analog computer utilizing a divider module.¶

Mean external cardiac work was calculated as the product of mean arterial pressure and cardiac output. For this computation only cardiac output was also calculated as the sum of ascending aortic blood flow measured by the electromagnetic flowmeter and estimated total coronary blood flow. Total coronary flow was estimated as three times left circumflex coronary blood flow, which was measured with flowmeters. Continuous records of LV dP/dt were derived from the LV pressure signal using an operational amplifier connected as a differentiator. A triangular wave signal with known slope was substituted for the pressure signal to calibrate the differentiator directly. In addition, by feeding the LV pressure signal to the Y axis and the diameter signal to the X axis of a storage oscillograph (Tektroniks 912) an instantaneous pressure diameter loop could be obtained. The instantaneous LV pressure diameter relationship could thus be analyzed on Polaroid pictures of selected beats.

The experiments were conducted 6–8 weeks after recovery from operation, when the dogs appeared vigorous and healthy. Continuous recordings of LV pressure, LV internal diameter, coronary blood flow, cardiac output, regional blood flow, arterial pressure and heart rate were obtained with the dogs lying in the right lateral position. The infusion of NP (Nipride)** was maintained for 7 min. Two doses of NP were selected: 2.5 µg/kg/min,¹⁰ which reduced mean arterial pressure by approximately 10%, and 25 µg/kg/min, which was the maximum dose consistently tolerated by the animals. In two dogs, while iliac blood flow and arterial pressure were monitored, a 7 min infusion of NP, 5 µg/kg/min, was immediately followed by an infusion of 25 µg/kg/min. In four dogs in which iliac blood flow and arterial pressure were measured NP, 2 µg/kg/min, was infused for 7 min directly into the iliac artery through an implanted catheter.

Results were compared with the preinfusion controls by use of the paired t-test, and responses in different vascular beds were compared by the unpaired t-test.²⁹

Results

The preinfusion control and maximal effects of NP hemodynamic data are presented in table 1. Since the effects of both doses of i.v. NP were qualitatively similar, only the effects of the 25 µg/kg/min infusion will be reported in detail. The intravenous administration of NP induced a time-dependent pattern of hemodynamic changes. The direct action of the drug was evident early during the infusion, i.e., during the first 3 min; following 5–7 min of infusion a new hemodynamic state was reached, characterized by the summation of direct effects with reflex adjustments. After discontinuation of the infusion, a slow recovery toward control occurred.

Systemic Circulation

The initial effect of NP was to reduce mean arterial pressure by 30 ± 3% (SEM) (P < 0.001) of control (fig. 1). By the end of the infusion period mean arterial pressure was 23 ± 3% (P < 0.001) below control. Cardiac output (minus coronary flow) initially increased by 39 ± 7% (P < 0.01), but had returned to control by the end of the infusion period; it fell by 16 ± 4% (P < 0.01) below control early during the recovery period. Likewise, total peripheral resistance (TPR) dropped initially by 42 ± 4% (P < 0.001) below control; by the end of the infusion period the reduction was only 28 ± 6% (P < 0.01) below control and it rose to reach a value of 17 ± 6% (P < 0.05) above control during recovery. The initial increases in cardiac output and decreases in TPR were actually slightly greater than measured, since coronary flow, which is not included in the cardiac output measurements, initially rose more than systemic flow. Heart rate increased initially by 101 ± 11%; late during the infusion it was 88 ± 20% above control (P < 0.01), and it returned promptly to control when the infusion was terminated. External cardiac work (per min) was not significantly changed early in the course of the infusion when arterial pressure and cardiac

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* Konigsberg Instruments (P22).
† Zepeda Instruments.
‡ Statham Instruments.
§ Benton Instruments.
¶ Teledyne Philbrick.

** Roche Laboratories.
Table 1. Maximal Effects of Nitroprusside

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Maximal change</th>
<th>Time (min) to peak effect</th>
<th>Maximal change</th>
<th>Time (min) to peak effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>94 ± 3</td>
<td>-13 ± 1*</td>
<td>3</td>
<td>-28 ± 3*</td>
<td>3</td>
</tr>
<tr>
<td>Cardiac output (L/min)</td>
<td>2.36 ± 0.09</td>
<td>0.34 ± 0.06*</td>
<td>1</td>
<td>0.94 ± 0.20*</td>
<td>1</td>
</tr>
<tr>
<td>Total peripheral resistance (mm Hg/L/min)</td>
<td>39.88 ± 2.98</td>
<td>-8.7 ± 1.6*</td>
<td>2</td>
<td>-17 ± 2*</td>
<td>1</td>
</tr>
<tr>
<td>External cardiac work (mm Hg/L/min)</td>
<td>218 ± 10</td>
<td>-18 ± 2*</td>
<td>10</td>
<td>-44 ± 13*</td>
<td>3</td>
</tr>
<tr>
<td>Mesenteric blood flow (ml/min)</td>
<td>236 ± 23</td>
<td>76 ± 11*</td>
<td>1</td>
<td>231 ± 54*</td>
<td>1</td>
</tr>
<tr>
<td>Mesenteric resistance (mm Hg/ml/min)</td>
<td>0.44 ± 0.05</td>
<td>-0.13 ± 0.01*</td>
<td>1</td>
<td>-0.26 ± 0.02*</td>
<td>1</td>
</tr>
<tr>
<td>Renal blood flow (ml/min)</td>
<td>158 ± 14</td>
<td>10 ± 4**</td>
<td>3</td>
<td>27 ± 17</td>
<td>7</td>
</tr>
<tr>
<td>Renal resistance (mm Hg/ml/min)</td>
<td>0.67 ± 0.04</td>
<td>-0.24 ± 0.04*</td>
<td>3</td>
<td>-0.24 ± 0.04*</td>
<td>7</td>
</tr>
<tr>
<td>Iliac blood flow (ml/min)</td>
<td>139 ± 16</td>
<td>10 ± 7</td>
<td>1</td>
<td>52 ± 8*</td>
<td>1</td>
</tr>
<tr>
<td>Iliac resistance (mm Hg/ml/min)</td>
<td>0.88 ± 0.16</td>
<td>-0.14 ± 0.06**</td>
<td>3</td>
<td>-0.40 ± 0.09*</td>
<td>1</td>
</tr>
<tr>
<td>Left circumflex coronary blood flow (ml/min)</td>
<td>54 ± 6</td>
<td>21 ± 7</td>
<td>1</td>
<td>121 ± 21*</td>
<td>1</td>
</tr>
<tr>
<td>Left circumflex coronary resistance (mm Hg/ml/min)</td>
<td>1.36 ± 0.17</td>
<td>-0.44 ± 0.08*</td>
<td>1</td>
<td>-1.02 ± 0.05*</td>
<td>1</td>
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<tr>
<td>Left ventricular peak pressure (mm Hg)</td>
<td>128 ± 6</td>
<td>-9 ± 2*</td>
<td>5</td>
<td>-18 ± 5*</td>
<td>3</td>
</tr>
<tr>
<td>Left ventricular end-diastolic pressure (mm Hg)</td>
<td>11 ± 1</td>
<td>-7 ± 1*</td>
<td>7</td>
<td>-9 ± 1*</td>
<td>3</td>
</tr>
<tr>
<td>Left ventricular maximum dP/dt (mm Hg/sec)</td>
<td>3161 ± 117</td>
<td>685 ± 186*</td>
<td>1</td>
<td>1277 ± 249*</td>
<td>1</td>
</tr>
<tr>
<td>Left ventricular end-diastolic internal diameter (mm)</td>
<td>37.3 ± 2.3</td>
<td>-5.2 ± 0.5*</td>
<td>3</td>
<td>-7.0 ± 0.6*</td>
<td>3</td>
</tr>
<tr>
<td>Left ventricular end-systolic internal diameter (mm)</td>
<td>30.7 ± 1.7</td>
<td>-3.4 ± 0.6*</td>
<td>3</td>
<td>-4.3 ± 0.5*</td>
<td>3</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>88 ± 2.7</td>
<td>38 ± 3*</td>
<td>3</td>
<td>89 ± 9*</td>
<td>1</td>
</tr>
</tbody>
</table>

*P < 0.01.  **P < 0.05.

Figure 1. Mean (± SEM) changes from control are shown for mean arterial pressure, cardiac output, total peripheral resistance and heart rate in six conscious dogs during infusion of sodium nitroprusside (NP) 2.5 μg/kg/min (closed triangles) for 7 min and then for the following 30 min. The period of infusion is indicated by the open bars, while significant changes from control are indicated by the symbols. While the drug induced primarily vasodilation during infusion, note the overshoot in total peripheral resistance during the recovery period.
output changed reciprocally; it was reduced by 20 ± 6% (P < 0.05) of control late during the infusion, when arterial pressure was still reduced and cardiac output was essentially back to control; after termination of the infusion it returned back to control levels in about 10 min. Similar results were obtained when cardiac work was calculated from the cardiac output figure, which included estimated total coronary blood flow, as well as measured ascending aortic blood flow.

Peripheral Circulation

Early during the infusion all beds displayed a significant vasodilation, with the renal bed displaying the least and the coronary beds the greatest response (fig. 2), renal blood flow increased by 10 ± 3% (P < 0.05), renal resistance was reduced by 27 ± 5% (P < 0.001); iliac blood flow increased by 38 ± 6% (P < 0.001), as resistance decreased by 43 ± 3% (P < 0.001); mesenteric blood flow increased by 98 ± 23% (P < 0.01), as resistance fell by 60 ± 4% (P < 0.001). Mean left circumflex (fig. 3) coronary blood flow increased by 225 ± 39% (P < 0.001), as resistance fell by 75 ± 4% (P < 0.01). By the end of the infusion period, while renal vasodilation was essentially unmodified from that observed earlier, dilation in the other beds was much less than observed early in the infusion. Resistance was only 35 ± 12% (P < 0.05) below control in the coronary bed and 32 ± 12% (P < 0.05) below control in the mesenteric bed; in contrast iliac blood flow was significantly reduced (−40 ± 9%, P < 0.01) and resistance was increased (33 ± 11%, P < 0.05) above control.

After the end of the infusion all the beds, with the exception of the renal, displayed a significant and sustained vasoconstriction (figs. 2, 3). Resistance rose above the preinfusion control values by 26 ± 10% (P < 0.05) in the mesenteric bed, to 90 ± 14% (P < 0.001) in the coronary bed, and 79 ± 23% (P < 0.05) in the iliac bed, while renal resistance returned slowly toward control, without any overshoot above control.

In order to determine if the iliac vasoconstriction could be overcome by a higher dose of the drug NP, 5 μg/kg/min, was infused i.v. to two dogs for 7 min and immediately followed by NP, 25 μg/kg/min. Just prior to increasing the dose of NP, mean arterial pressure was 4% and 37% and iliac flow was 25% and 50% below control respectively in the two dogs, while iliac resistance had risen by 28% and 25% above control. Within 1 min of the higher dose, mean arterial pressure fell to values of 40% and 47% below control, while iliac flow rose and the iliac vasoconstriction was reversed to dilation, i.e., iliac resistance fell to values of 28% and 25% below control respectively in the two experiments.

In order to determine if the iliac vasoconstriction was a direct or a reflex effect of the drug, NP, 2 μg/kg/min, was infused into the iliac artery to four conscious dogs. With direct i.a. infusion mean arterial pressure fell negligibly, while iliac flow rose and resistance fell initially by 54 ± 6% and remained depressed, although slightly less, during the remainder of the 7 min infusion period. Iliac resistance was still depressed by 49 ± 6%, (P < 0.01) at 7 min, just prior to termination of the infusion and returned to control during the recovery period. In contrast to the effects of i.v. administration, iliac vasoconstriction was not observed (fig. 4).
**Figure 3.** A typical recording of phasic and mean arterial pressure, left circumflex coronary flow, calculated mean coronary resistance, and heart rate is shown in a conscious dog during a 7 min i.v. infusion of 25 μg/kg/min of NP (indicated by the arrows) and early in the recovery phase. Note the marked vasodilation during the vasoconstriction after the infusion.

**Figure 4.** The effects of NP, 25 μg/kg/min, i.v. (triangles) and 2 μg/kg/min i.a. (circles) are compared on average ± SEM measurements for iliac flow and resistance. While both infusions elicited initial and similar degrees of iliac vasodilation, only the i.v. dose was characterized by a later phase of iliac vasoconstriction. This later phase of iliac vasoconstriction was presumably due to reflex action, since it was not observed when NP was infused directly into the iliac artery.

**Left Ventricular Dynamics**

In contrast to the effects observed in the regional beds, changes in LV dynamics were more stable throughout the 7 min infusion period (figs. 5, 6). LV systolic pressure fell by 14 ± 3% (P < 0.01), LV end-diastolic pressure was reduced by 9.1 ± 0.1 from 11 ± 1 mm Hg. Left ventricular end-diastolic diameter decreased by 17 ± 2% (P < 0.01), while end-systolic diameter fell by 13 ± 2% (P < 0.001) and the extent of myocardial fiber shortening per stroke fell by 31 ± 3% (P < 0.001). All of these changes slowly returned to control by 15 min after the termination of the infusion. LV max dP/dt transiently rose by 41 ± 8% (P < 0.01) above control during the early phase of the infusion, then declined and fell to levels 13 ± 3% (P < 0.05) below control following termination of the infusion.

The importance of tachycardia in mediating LV responses to NP was tested in five animals. Atrial pacing at 150 beats/min decreased the LV end-diastolic pressure from 12.4 ± 0.8 mm Hg to 6.3 ± 1.2 mm Hg (P < 0.01), and LV end-diastolic diameter from 39.32 ± 1.79 mm to 36.30 ± 1.87 mm (P < 0.01), while end-systolic diameter was not significantly affected. Nitroprusside infusion further reduced LV end-diastolic pressure to 2.0 ± 1.2 mm Hg (P < 0.01), LV end-diastolic diameter to 33.08 ± 2.01 mm and LV end-systolic diameter to 27.01 ± 2.40 mm. The reductions in cardiac size and LV end-diastolic pressure induced by NP with heart rate kept constant by pacing were significantly less (P < 0.01) than when heart rate was allowed to vary, indicating that in part the mechanism of the NP induced decrease in cardiac size was due to the concomitant tachycardia.

The dynamic relationship between LV pressure and diameter during diastole, as reflected by instantaneous pressure-diameter plots, was not appreciably altered by the intravenous infusion of NP (fig. 7).
Discussion

The present study characterizes the sequence of hemodynamic changes produced by an intravenous infusion of NP in the normal, conscious dog. The effects, particularly in the peripheral circulation, were found to vary considerably with time.

The changes in the various systemic vascular beds observed with the infusion of NP varied as a function of time, similar to the effects of nitroglycerin. For example, during the first three minutes, there was a marked overall vasodilation in the systemic circulation as well as in each of four regional beds studied. Presumably this initial effect reflects primarily the direct relaxant action of the drug on vascular smooth muscle. The observation that the cardiac output increased early during the infusion of the drug, then

Figure 5. A typical recording of phasic left ventricular (LV) pressure, dP/dt, internal diameter, dD/dt, i.e., velocity of shortening, mean arterial pressure and heart rate in a conscious dog during 7 min i.v. infusion of 25 µg/kg/min of NP (indicated by the arrows) and the early recovery period. Note the marked reduction in left ventricular dimensions during infusion: end-diastolic size (preload) is equivalent to end-systolic size prior to NP.

Figure 6. Mean (± SEM) changes from control during 7 min i.v. infusion of NP on LV systolic pressure, max dP/dt, end-diastolic and end-systolic internal diameters in seven conscious dogs. Significant changes from control are denoted by symbols. Note the marked and persistent reduction in LV dimensions, as opposed to the transient increase in dP/dt.
returned to control with continued infusion and fell below control after the discontinuation of the infusion of NP, may well explain the variability of responses observed in studies in normal human subjects. The importance of the baseline level of hemodynamic performance is emphasized by those studies showing a consistent increase in cardiac output when the drug is given under conditions in which myocardial performance is depressed either by disease or anesthesia both in experimental animals and in patients.

Interestingly, peripheral blood flow did not increase uniformly in the different beds. This finding might reflect a differential sensitivity of the various beds to NP, the renal bed being the least sensitive to the four beds studied. The various beds also varied in their responses as a function of the duration of infusion. While vasodilation persisted in the renal, coronary, and mesenteric vascular beds, and in the overall systemic circulation, late during the infusion period an actual increase in resistance was observed in the iliac bed. This increase in resistance could be overcome by increasing the dose of the infusion. After cessation of the infusion a prolonged period of vasoconstriction ensued. Total peripheral resistance as well as coronary, mesenteric, and iliac resistances were all increased, while only the renal bed failed to constrict.

This vasoconstriction, in beds other than the renal, is most likely reflex in nature, and presumably is secondary to activation of baroreflex mechanisms. This interpretation is supported by the experiments in which 2.0 μg/kg/min of NP was infused directly into the iliac artery through an implanted catheter. In this case, in which systemic effects were negligible, an initial reduction of iliac resistance of 54 ± 6% was observed, very similar to the initial iliac vasodilation observed with the 25 μg/kg/min i.v. dose. In contrast to the results from the i.v. NP experiments, iliac resistance was still 49 ± 6% below control at 7 min, just prior to cessation of the infusion and after the infusion was discontinued iliac resistance returned to, but not above control. A similar vasodilation has been observed with an infusion of NP into the cerebral circulation of the conscious goat. These findings all lend support to the concept that the peripheral vascular effects of NP are the result of several interacting forces, e.g., the direct vasodilating effects of the drug, secondary reflex effects elicited by the reductions in arterial and cardiac pressure, and local autoregulatory effects in the individual beds possibly involving tachyphylaxis.

The cardiac effects of infusion include a pronounced tachycardia and a sustained and marked reduction in left ventricular diameter. While an increase in heart rate has previously been described in normal animals and in normal human subjects, heart rate usually exhibits little change in patients with congestive heart failure. This might be related to a reduced sensitivity of the baroreceptor reflex and the impairment of control of the sinoatrial rate by the autonomic nervous system in chronic congestive heart failure. The reductions in left ventricular dimensions induced by NP reflect the effects of both tachycardia and of the decreases of both preload and afterload. The drug induces venodilation which undoubtedly contributes to the reduction in preload. Following cessation of the infusion, left ventricular diameter remained depressed, at a time when heart rate had returned to control, indicating a persistent venodilation. The reduction of arterial pressure and of ventricular dimensions indicate reduced preload and afterload, factors which might be expected to reduce myocardial oxygen requirements. On the other hand, the tachycardia and the increase in myocardial contractility, reflected in the increase in left ventricular dP/dt, would counteract this effect.

The dynamic pressure-diameter relationship of the left ventricle during diastole (fig. 7) was not altered by NP, suggesting that the compliance of the normal canine ventricle is not affected. Similarly, in human subjects without congestive heart failure, NP does not modify the diastolic pressure-volume relations of the left ventricle, while in patients with heart failure these relations are shifted so that a lower end-diastolic pressure occurs at any given volume, i.e., an increase in compliance is observed. The mechanism responsible for this shift is not clear.

In conclusion, intravenous NP induces a complex, time-dependent pattern of hemodynamic changes in the conscious dog. While a transient, generalized vasodilation is observed early after the onset of infusion, later during the infusion a new hemodynamic state is reached, apparently modified by reflex adjustments. Mesenteric and coronary vasodilation are reduced at this time, while an actual vasoconstriction is observed in the iliac bed, which displays an increase in resistance even during the infusion of the drug.

References

5. Grossman W, Harshaw CW, Munro AB, Becker L, McLaurin LP.
30. Ivanovich AD, Miletich DJ, Albrecht RF, Zahed B: Sodium nitroprusside and cerebral blood flow in the anesthetized and anesthetized goat. Anesthesiology 44: 21, 1976
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