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Some Hemodynamic Effects of Sodium Nitroprusside

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Arterial hypotension to about 45 mm Hg below control was induced in 12 patients by infusion of a 0.01 per cent solution of sodium nitroprusside. The drug was found reliable, free of tachyphylaxis, and evanescent of action. During the hypotensive phases arterial oxygen saturation was maintained at 95–99 per cent. Cardiac output decreased insignificantly by a mean value of 200 ml/min in conscious individuals, but increased by about 850 ml/min in anesthetized subjects. Blood pressures returned to 90 per cent of control values within 120 seconds of discontinuation of sodium nitroprusside. The use of the drug merits further investigation. (Key words: Hypotension; Sodium nitroprusside; Available oxygen.)

THE CARDIOVASCULAR EFFECTS of sodium nitroprusside in normotensive and hypertensive patients have been described by Schlant *et al.*,[1] and those following acute myocardial infarction, by Franciosa *et al.*[2] Two clinical studies of the use of this drug as a hypotensive agent in anesthetic practice have been published.[3, 4] Schlant *et al.*[1] reported a 37.2 per cent reduction in mean arterial blood pressure in normotensive patients given intravenous doses of 0.61–3.87 μg/kg/min sodium nitroprusside. This was associated with a mean decrease of peripheral vascular resistance of 31.1 per cent, an 8.8 per cent decline in cardiac index, and an increase in heart rate of 5.5 per cent. These effects and the hemodynamic changes found in patients given sodium nitroprusside after myocardial infarction[2] suggest that the drug is a pure vasodilator, without action upon the heart or sympathetic nervous system.[1, 5] Reports of the use of sodium nitroprusside as a hypotensive agent in clinical anesthetic practice[3, 4] stress the potency, evanescence of action, and absence of tachyphylaxis of the drug, and suggest that further evaluation is indicated.

The availability of oxygen to the tissues, an important factor in clinical anesthetic practice, merits special attention during induced hypotension, because in this situation cardiac output is commonly reduced.[6–8] There are no published reports of the effects of sodium nitroprusside on cardiac output or arterial oxygenation in anesthetized man. In this study an attempt has been made to augment available knowledge by providing this information.

Methods

Twelve patients, five women and seven men, were investigated, with their consent. Patients were 20 to 50 years old and had no clinical evidence of cardiopulmonary or central nervous system disease. In every case elective surgery involving structures close to the body surface was indicated, and the surgeons had requested that arterial blood pressures be controlled during these procedures. Surgical procedures included excision of facial keloid malformations and lipomata and a salivary gland exploration. All studies were performed with the patients supine in the horizontal position.

Patients received 100 mg pethidine (meperidine) and 25 mg promethazine intramuscularly 30 to 60 minutes before the study. Using local analgesia, plastic catheters were inserted percutaneously into the radial artery, and into the right atrium from a right antecubital vein. Pressures were measured by Statham strain-gauge transducers supported 3 inches above the surface of the operating table and recorded continuously on a Philips 3T recorder. Heart rate was measured using a SAN-El-

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TABLE I. Hemodynamic Data from Five Patients (Group I) Given Sodium Nitroprusside after Control Periods before and after Induction of Anesthesia*

	Control, Awake	Sodium Nitroprusside Hypotension, Awake	Control, Awake	Control, during Anesthesia	During Anesthesia and Sodium Nitroprusside	During Anesthesia after Sodium Nitroprusside
Blood pressure (mm Hg)	92.4 ± 7.3	48 ± 8.7‖	79.5 ± 5.7	89.6 ± 6.4	46.5 ± 4.6‖	90 ± 14.1
Heart rate (beats/min)	70.6 ± 11.8	70.2 ± 19.7	51 ± 2.2	80.6 ± 11.1	93.2 ± 10.3‡	66.7 ± 12.3
Central venous pressure (mm Hg)	4 ± 0.3	1 ± 0.25†	4 ± 0.21	2 ± 0.2	0 ± 0.13†	2 ± 0.14
Cardiac output (l/min)	4.3 ± 0.3	4.1 ± 0.3	3.6 ± 0.2	4.4 ± 1.2	5.3 ± 0.9	3.8 ± 0.4
Stroke volume (ml)	63 ± 13.2	62 ± 15	70 ± 7.5	54 ± 10.5	57 ± 10.7	49 ± 3.7
Peripheral vascular resistance (dynes/sec/cm^{-5})	1,721 ± 226	931 ± 156§	1,708 ± 61	1,722 ± 333	712 ± 79¶	1,913 ± 180
Oxygen saturation (per cent)	97 ± 2.1	97 ± 1.3	97 ± 2.4	99 ± 3.5	99 ± 3.7	98 ± 3.1
Available oxygen (ml/min)	766 ± 93	751 ± 108	665 ± 90	824 ± 315	904 ± 196	683 ± 71
Pa_{O_2} (mm Hg)	95 ± 10.5	93 ± 11.2	95 ± 11.1	120 ± 28.2	110 ± 17.9	135 ± 25.3
Pa_{CO_2} (mm Hg)	40 ± 3.7	37 ± 4.2	41 ± 4.7	40 ± 4.5	39 ± 3.9	42 ± 4.2
*p*H	7.41 ± 0.07	7.39 ± 0.06	7.4 ± 0.08	7.37 ± 0.05	7.35 ± 0.06	7.40 ± 0.07
$P\bar{v}_{O_2}$ (mm Hg)	45 ± 3.7	47 ± 3.8	45 ± 3.0	50 ± 4.3	49 ± 4.8	45 ± 7.1
$P\bar{v}_{CO_2}$ (mm Hg)	47 ± 5.0	42 ± 2.7	47 ± 4.5	48 ± 4.7	43 ± 5.0	47 ± 3.7
*p*H	7.37 ± 0.03	7.30 ± 0.05	7.30 ± 0.04	7.30 ± 0.05	7.30 ± 0.05	7.35 ± 0.07

* Results are means ± SD. Statistical data relate to comparison of values obtained during infusion of sodium nitroprusside with those obtained in the preceding control period.
† $P < 0.05$; ‡ $P < 0.025$; § $P < 0.01$; ¶ $P < 0.005$; ‖ $P < 0.001$.

2D16 pulsemeter and a finger photocell. Cardiac output was measured by dye dilution using indocyanine green and the Philips XO-1000 combined oximeter/densitometer cuvette. Arterial oxygen saturation and hemoglobin were measured during the cardiac output estimation. Blood needed for estimating acid–base and blood–gas status was obtained from the arterial and venous catheters at regular intervals during the studies, and analyzed in duplicate, using the Beckman modular blood–gas assembly.

At the conclusion of each experiment the cardiac output densitometer was calibrated using the patient's own blood and known doses of indocyanine green. Cardiac output was calculated using the method of Williams *et al.*[9] to prepare an appropriate program for an Olivetti digital computer. Total peripheral vascular resistance (PVR) was calculated from the formula of Aperia [10]:

$$PVR = \frac{\text{mean arterial pressure (mm Hg)}}{\text{cardiac output (l/min)}} \times 80 \text{ dynes sec cm}^{-5}$$

Available oxygen was calculated from the formula:

$$\text{Available oxygen (ml/min)} = \frac{\text{cardiac output ml/min} \times (\text{hemoglobin} \times 1.34)}{100} \times \% \text{ oxygen saturation}$$

Tests of statistical significance were applied to the mean differences between values obtained in the control periods preceding hypotension and during the hypotensive phases, induced by halothane on the one hand, and sodium nitroprusside on the other, by applying Student's t test to the paired comparisons.

Five patients (Group I) received sodium nitroprusside after control periods both before and after induction of anesthesia. Patients were left undisturbed following introduction of the catheters until heart rates and arterial pressures were steady. Cardiac output, arterial oxygen saturation and hemoglobin estimations were then made at about 3-minute intervals until the areas of at least two dye-dilu-

TABLE 2. Hemodynamic Data from Seven Patients (Group II) Given Sodium Nitroprusside after Induction of Anesthesia

	Control during Anesthesia	Value during Sodium Nitroprusside Hypotension	Control
Blood pressure (mm Hg)	99.7 ± 13.6	54.6 ± 11.7‖	95.7 ± 10.8
Heart rate (beats/min)	88.0 ± 22	113.0 ± 25†	78.4 ± 20.6
Central venous pressure (mm Hg)	2 ± 0.3	1 ± 0.2†	4 ± 0.5
Cardiac output (l/min)	4.3 ± 1.1	5.1 ± 1.0	4.0 ± 0.8
Stroke volume (ml)	50 ± 10	47 ± 14.8	48 ± 9.3
Peripheral vascular resistance (dynes sec cm^{-5})	1,930 ± 485	917 ± 386‖	1,913 ± 456
Oxygen saturation (per cent)	95 ± 2.1	95 ± 2.3	96 ± 2.3
Available oxygen (ml/min)	665 ± 82	803 ± 220	632 ± 72
Pa_{O_2} (mm Hg)	92 ± 17.1	85 ± 18.3	95 ± 13.7
Pa_{CO_2} (mm Hg)	35 ± 7.4	30 ± 7.7	37 ± 8.0
*p*H	7.37 ± 0.05	7.39 ± 0.04	7.37 ± 0.06
$P\bar{v}_{O_2}$ (mm Hg)	41 ± 9.1	40 ± 7.1	42 ± 5.3
$P\bar{v}_{CO_2}$ (mm Hg)	42 ± 7.3	37 ± 5.8	49 ± 3.7
*p*H	7.31 ± 0.02	7.30 ± 0.07	7.30 ± 0.06

* Results are means ±SD. Each period of hypotension was preceded by a control period. Statistical data relate to comparison of values obtained during infusion of sodium nitroprusside with those obtained in the preceding control period.

† $P < 0.05$; ‡ $P < 0.025$; § $P < 0.01$; ¶ $P < 0.005$; ‖ $P < 0.001$.

tion curves appeared to agree within 10 per cent and the arterial oxygen saturation was steady to within 1 per cent. Blood pressures and heart rates at this moment were recorded and served as control measurements. Infusion of a 0.01 per cent solution of sodium nitroprusside in 5 per cent dextrose in water was then commenced, at a rate adjusted to maintain the mean arterial blood pressure between 40 and 50 mm Hg below the control level. When the hypotensive state had been established for at least 5 minutes, all hemodynamic measurements were repeated. Infusion of sodium nitroprusside was then discontinued and a second series of control estimations was made when the blood pressure returned to control levels.

Anesthesia was induced by 100 to 200 mg of 2.5 per cent thiopental given intravenously over a period of 30 seconds. All patients received 50 mg succinylcholine intravenously to facilitate intubation of the trachea. Continued apnea was achieved by giving each patient either alcuronium or pancuronium. Patients were connected to a Manley respirator delivering an expired minute volume of about 5 liters (70 per cent nitrous oxide and 30 per cent oxygen). The minute volume was adjusted as necessary to Pa_{CO_2} between 30 and 40 mm Hg. A period of 10 minutes was allowed to elapse following induction of anesthesia and then control hemodynamic measurements were made. After incision of the skin, sodium nitroprusside infusion was commenced, and when mean blood pressure was 40–50 mm Hg below the control level, all hemodynamic measurements were repeated. Surgical intervention was interrupted 3 minutes prior to measurement periods. Sodium nitroprusside infusion was discontinued to coincide with surgical needs, and when the arterial blood pressure had approximated control values for at least 15 minutes, a final series of control measurements was made.

Seven patients (Group II) were investigated after induction of anesthesia. The initial anesthetic management and methods of study were identical to those described above.

Results

Hypotension was readily obtained following the infusion of sodium nitroprusside, although some difficulty in obtaining a steady level of reduced mean pressure was experienced initially. The surgeons were well satisfied with operating conditions in all cases.

Group I patients were unaware of the reductions in their blood pressures preoperatively, and experienced no ill effects whatever.

The average reduction of mean arterial pres-

sure during sodium nitroprusside infusion (44 mm Hg) was associated with significant decreases in central venous pressure and peripheral vascular resistance (table 1). Cardiac output and arterial oxygen saturation were not changed, indicating that available oxygen was maintained at control levels.

Responses to sodium nitroprusside during anesthesia differed significantly from those in the conscious state in respect to heart rate, which increased by 13 beats/min, only. In addition, mean cardiac output increased by 900 ml/min and mean available oxygen increased by more than 75 ml/min, but these changes were not significant.

In Group II, responses to sodium nitroprusside were similar in every respect to those in Group I following induction of anesthesia (table 2).

There was no notable change in the blood–gas or acid–base status of patients during this study except a slight increase in Pa_{CO_2} following induction of anesthesia (tables 1 and 2). Arterial hypotension, once established, was readily maintained by a fixed rate of sodium nitroprusside infusion, indicating that there was no early tendency to develop tachyphylaxis.

Following discontinuation of sodium nitroprusside, arterial blood pressure returned to within 90 per cent of control in less than 120 seconds in all cases.

Discussion

Major considerations in induced hypotension are oxygenation and the adequacy of blood flow, particularly to the brain. A technique which provides good surgical conditions without a reduction in available oxygen is preferable to one known to reduce cardiac output and available oxygen.

Clinical studies [3, 4] indicate that sodium nitroprusside provides good surgical conditions. Results of the present study indicate that these conditions are obtained without jeopardizing oxygen delivery, and further suggest that reduction of *arterial pressure* rather than *blood flow* is the factor that facilitates surgery in induced hypotension. Venous blood *p*H and blood–gas, although not strictly representative of mixed venous blood, were maintained at control levels during the hypotensive phases of the study, suggesting that total-body perfusion was adequate. In contrast, when hypotension is induced by ganglionic blocking drugs, spinal anesthesia, or deep halothane anesthesia, cardiac output is reduced.[6, 7, 8, 11] Halothane and trimethaphan, probably the most popular sequence, were associated in one study with a significant 11.8 per cent reduction in cardiac output,[6] and in another with 33–41 per cent reductions in cardiac index.[7]

It is concluded that sodium nitroprusside may offer important advantages as a hypotensive agent and merits further scrutiny in depth regarding, for example, adequacy of regional perfusion of vital organs.

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