Sodium Nitroprusside Increases $Q_s/Q_t$ in Dogs with Regional Atelectasis

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This study investigated the effects of sodium nitroprusside (SNP) on arterial oxygen tension ($P_{O_2}$), pulmonary shunt ($Q_s/Q_t$), and pulmonary vascular resistance (PVR) in the presence of atelectasis of one lung. Ten dogs were anesthetized, their tracheas intubated with a bronchial divider, and their lungs ventilated with IPPB with pure oxygen. Atelectasis of the left lung was produced by occluding the left side of the bronchial divider and ventilating the right lung. SNP was infused to decrease mean arterial blood pressure by 25 per cent. $P_{O_2}$ decreased from (mean value ± 1 SD) 134 ± 75 to 77 ± 23 torr ($P < 0.05$) with SNP infusion. $Q_s/Q_t$ increased from 30 ± 7.0 to 39 ± 6.0 per cent ($P < 0.05$), while cardiac output did not change significantly. PVR in the atelectatic lung decreased, while PVR on the ventilated lung was unchanged. The decrease in PVR in the atelectatic lung suggests that SNP decreases $P_{O_2}$ and increases $Q_s/Q_t$ by reversing the hypoxic pulmonary vasoconstriction. As a result, during SNP infusion, perfusion of the atelectatic lung was maintained while perfusion of the ventilated lung decreased. (Key words: Anesthetic techniques, hypotension, induced, nitroprusside; Lung, atelectasis; Lung, shunting; Lung, hypoxic vasoconstriction.)

SODIUM NITROPRUSSIDE is a hypotensive agent currently being used to diminish bleeding in anesthetized patients and to decrease myocardial afterload in patients with heart failure. Nitroprusside has minimal effect on myocardial contractility, but reduces systemic vascular resistance, resulting in lowered blood pressure.1 Its effect on the pulmonary circulation and blood-gas exchange has aroused interest because of observed decreases in $P_{O_2}$ associated with its use. Wildsmith et al.2 administered nitroprusside to anesthetized patients and found marked decreases in arterial oxygen tension ($P_{O_2}$) values in patients with low preoperative $P_{O_2}$ values and in older patients, suggesting a worsening of abnormal ventilation-perfusion ratios. The mechanism by which $P_{O_2}$ values decreased was not determined. Recently, we administered nitroprusside to a patient who had had an inadvertent intubation of the right mainstem bronchus and had a poorly ventilated or collapsed left lung. Nitroprusside infusion was associated with a decrease in $P_{O_2}$ from 105 to 50 torr with the patient breathing 40 per cent oxygen. The absence of information about the effects of nitroprusside on intrapulmonary shunting ($Q_s/Q_t$) and pulmonary blood flow distribution in the presence of regional atelectasis prompted this study.

Methods and Materials

Ten mongrel dogs, each weighing 24–27 kg, were anesthetized with pentobarbital 30 mg/kg, iv, placed in the supine position, and a double-lumen endotracheal tube (Rusch) was inserted through a tracheostomy. An animal respirator‡ was used to ventilate the lungs at a tidal volume of 15 ml/kg with pure oxygen. Succinylcholine, 100 mg, intramuscularly, was given to facilitate control of respiration. Catheters were advanced via a femoral artery into the abdominal aorta, and via a femoral vein into the inferior vena cava. A Swan-Ganz flow-directed catheter was passed via a jugular vein into the pulmonary artery and positioned so that a wedge pressure tracing could be obtained when the balloon was inflated. Femoral artery (AP), pulmonary artery (PAP), and airway (P_airway) pressures were monitored continuously and pulmonary wedge pressure (PAW) was measured intermittently.

Atelectasis of the oxygen-filled left lung was produced by occluding the lumen of the left side of the double-lumen tube, which was in turn connected to an underwater seal. The right lung was ventilated with pure oxygen at a tidal volume of 15 ml/kg and the respiratory rate set to maintain an arterial carbon dioxide tension ($P_{CO_2}$) between 30 and 40 torr. Separation of the right and left lungs was determined by the absence of bubbles in the underwater seal during positive-pressure ventilation of the right lung and by intermittently monitoring pressure changes in the occluded airway. Confirmation of collapse of the lung was determined post mortem.

Blood samples from the femoral and pulmonary arteries were analyzed immediately after collection for $P_{O_2}$, $P_{CO_2}$, and $pH§$ and hemoglobin content.¶ A Severinghaus slide rule was used to determine oxygen saturation of arterial and mixed venous blood for calculating oxygen content where $C_{O_2} = \text{per cent}$

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‡ Harvard. Model 60.
§ Instrumentation Laboratories (IL) model 113 pH/Gas Analyzer.
¶ Co-Oximeter model 182.
saturation \( \times \text{Hb} \times 1.34 + 0.0031 \text{P}_{\text{O}_2} \). Intrapulmonary right-to-left shunt \( (Q_r/Q_l) \) was determined using the standard oxygen method. Cardiac output \( (Q_c) \) was measured with the dye-dilution technique using indocyanine green dye. Pulmonary vascular resistance (PVR) in dynes-sec-cm\(^{-5}\) was calculated using the formula \( \text{PVR} = (\text{PAP} - \text{PAW}) \times 80/Q_c \). In calculating the PVR of each lung separately, the driving pressure across each lung was assumed to be the mean pulmonary arterial pressure (PAP) minus the pulmonary-artery wedge pressure (PAW). The flow to both lungs was taken to be the total cardiac output (Qc). Flow to the collapsed lung was assumed to equal the shunt flow (Qr). Flow to the ventilated lung (Qv) was calculated by subtracting Qr from Qc.

Measurements of Qr/Qc were made prior to occluding the left side of the double-lumen endotracheal tube to be sure that atelectasis was minimal in both lungs, and then at ten-minute intervals following occlusion. Control measurements for sodium nitroprusside infusion were performed 35–45 minutes after occluding the left lumen of the endotracheal tube. Sodium nitroprusside, .01 per cent, was then infused until the mean arterial pressure was decreased by 25 per cent. The total dose range of nitroprusside was 5–15 \( \mu g/\text{kg}/\text{min} \). After 10 minutes at the reduced pressure, measurements were repeated. Nitroprusside infusion was then stopped, blood pressure allowed to return to control levels, and the measurements repeated. Hemodynamic and blood-gas values resulting from nitroprusside infusion were compared with values found both before and after infusion of nitroprusside using Student's \( t \) test for paired data. At the end of the experiment the animals were sacrificed by intravenous administration of pentobarbital and the thoraces opened with the animals still being ventilated. In all animals we found that the left lung was completely collapsed and that the right or ventilated lung had no area of atelectasis.

**Results**

With both lungs being ventilated, Qr/Qc was 7.2 \( \pm \) 1.6 per cent (mean \( \pm \) SD). Qr/Qc increased to 30 \( \pm \) 7 per cent 35–45 minutes after bronchial occlusion, increasing rapidly during the initial 10–20 minutes but changing very little in the ten-minute period prior to nitroprusside infusion. Nitroprusside caused a significant decrease in Pa02 (\( P < 0.05 \)) of 57 torr; Pa02 reverted to control values (143 \( \pm \) 82 torr) when nitroprusside infusion ceased. Cardiac output (Qc) and mixed venous oxygen saturation (Sw02) did not change significantly (table 1). Qr/Qc, however, showed a marked increase from 30 \( \pm \) 7 to 39 \( \pm \) 6.0 per cent, reverting to 25 \( \pm \) 6.0 per cent after nitroprusside was stopped. The increase in Qr/Qc was associated with a 37 per cent decrease in PVR of the atelectatic lung, which served to maintain flow (Qr) to that lung in the face of a decrease in driving pressure (PAP – PAW). Flow to the ventilated lung (Qv), however, decreased 24 per cent (\( P < 0.05 \)), with no change in its PVR.

**Discussion**

We wished to determine the effects of nitroprusside infusion on blood-gas exchange and pulmonary blood flow distribution in the presence of regional atelectasis. In dogs with a collapsed left lung, we found that Pa02 values decreased markedly when nitroprusside was infused to lower mean arterial pressure by 25 per cent. On the basis of the low value for Qr/Qc prior to collapse and the postmortem finding that there was no atelectasis in the ventilated lung, we believe that the values for Qr found with and without nitroprusside represented only flow to the collapsed lung. Pa02 values decreased because nitroprusside caused a marked decrease in PVR of atelectatic lung with
no effect on PVR in the ventilated lung. As a result, shunt flow (Qs) was maintained to the atelectatic lung in the face of a decrease in driving pressure (PAP – PAW), flow to the ventilated lung (Qv) decreased, and the shunt fraction (Qs/Qv) increased.

The accuracy of our values for individual lung blood flows, Qs and Qv, and for individual lung vascular resistances, PVRs and PVRv, depends upon how closely the oxygen method measures only flow to the collapsed lung. The oxygen method normally determines flow through any unventilated areas plus unoxgenated blood flow in the theshian, bronchial, and pleural circulations. These flows, however, are normally a small fraction (1–5 per cent) of the total cardiac output. The oxygen method should thus accurately reflect alterations in flow to a collapsed lung that produce a large shunt of 30–40 per cent when the opposite lung is fully expanded. We determined the accuracy of this assumption by comparing shunt flow determined by the oxygen method with flow values to a collapsed lung determined by radioactive microspheres, a method that would not include flows outside the collapsed lung. In a similar animal preparation, values for flow to the collapsed lung determined by the oxygen method before and after hypotension induced by hemorrhage were found to be nearly identical (r = 0.95) to the values determined by radioactive microspheres injected into the pulmonary artery. If there were significant atelectasis in the ventilated right lung, then the oxygen method would not accurately reflect changes in flow to the collapsed left lung and our calculated values for PVR in each lung would be in error. We doubt that this is the case because 1) the value for Qs/Qv prior to left lung collapse was only 7.2 ± 1.6 per cent, indicating that there was minimal atelectasis in both lungs at that time; 2) the right lung subsequently was hyper-inflated, receiving a tidal volume of 15 ml/kg at the time the left lung was collapsed; 3) postmortem examination failed to reveal atelectasis in the right lung.

The effects of nitroprusside on the pulmonary circulation and blood-gas exchange would appear to depend on the extent of change in pulmonary vascular tone caused by ventilation-perfusion abnormalities and on the presence of increased pulmonary vascular pressures caused by myocardial failure. Nitroprusside appears to have little effect on pulmonary vascular resistance and Qs/Qv in the presence of normal ventilation-perfusion ratios, normal Qs/Qv, and normal pulmonary vascular pressures. Chatterjee et al.6 found that nitroprusside caused only insignificant decreases in PVR when infused into patients with normal left ventricular filling pressure (LVFP) and normal values for PVR, but marked decreases in PVR when infused into patients with increased LVFP (>15 torr) and PVR. In patients who had increased pulmonary vascular pressure secondary to myocardial failure, PVR may have decreased because cardiac output increased, causing mechanical dilatation of vessels, rather than because of a direct vasodilatory effect of nitroprusside on the pulmonary circulation. Styles et al.7 infused nitroprusside into patients anesthetized with nitrous oxide, 70 per cent, and oxygen, 30 per cent, with normal cardiopulmonary function and found insignificant decreases in PaO2 (92 ± 17.1 to 85 ± 18.3 torr, mean ± SD). Stone et al.8 found that nitroprusside had no effect on PaO2 or Qs/Qv in patients with normal lungs breathing halothane and nearly pure oxygen. The patients in this study had a control value for PaO2 of 625 ± 14 torr, mean ± SEM, and a control Qs/Qv of 4.2 ± 1.0 per cent. The inhalation of pure oxygen would have prevented any effect of low ventilation-perfusion ratios on vascular tone, and the low Qs/Qv indicates the absence of significant atelectasis in these patients.

Wildsmith,2 however, found that nitroprusside produced significant decreases in PaO2 (180 ± 59 to 133 ± 75 torr, mean ± SD) when infused into patients undergoing otolaryngologic operations anesthetized with 50 per cent nitrous oxide and oxygen with halothane. Decreases in PaO2 were more marked in patients with lower preoperative PaO2 values and in older patients. Wildsmith suggested that the effect of nitroprusside in lowering PaO2 values increased with increasing ventilation-perfusion scatter. Seltzer et al.9 also found that nitroprusside produced significant decreases in PaO2 (219 ± 47.9 to 143.1 ± 34.1) when infused into patients undergoing coronary-artery operations under morphine-nitrous oxide anesthesia (50:50).

Our study confirms the findings of Wildsmith et al.2 and Seltzer et al.9 that nitroprusside, when given to produce systemic hypotension, can alter pulmonary gas exchange, and indicates that one mechanism is by causing a disproportionate decrease in vascular resistance in unventilated areas of lung.

In the presence of a collapsed lung, we postulate two means by which nitroprusside might increase Qs/Qv. SNP is a known dilator of systemic vessels.10 Our results suggest that SNP preferentially dilates vessels perfusing unventilated lung. Its marked effect in decreasing vascular resistance in the atelectatic lung may be due to the reversal of increased
vascular tone induced by hypoxic vasoconstriction. Arkin et al.** found that nitroprusside restored flow to lung in which hypoxic vasoconstriction was induced by nitrogen ventilation, demonstrating that nitroprusside can inhibit hypoxic vasoconstriction. Collapsing a lung has been shown to result in an increase in vascular resistance that is due both to narrowing of large vessels and to an increase in vasomotor tone (hypoxic pulmonary vasoconstriction) induced by alveolar hypoxia. That hypoxic vasoconstriction existed in our animals is suggested by the relatively low value of 30 per cent Q/A representing primarily flow through the collapsed left lung. Normally the inflated left lung in the dog receives 40 per cent of the cardiac output.13

A second means by which nitroprusside might increase Q/A in this model is by decreasing pulmonary intravascular pressure, causing disproportionate changes in resistance in the two lungs. When pulmonary intravascular pressure is decreased by hemorrhage, pulmonary vascular resistance tends to increase due to compression of vessels by alveolar pressure, especially at the top of the lung, where the hydrostatic pressure is lowest.14 This effect would be more marked in the ventilated lung, where alveolar pressure and lung height are high, and minimized in the collapsed lung, where lung height and alveolar pressure are low. We found in the supine dogs in this study that the height of the atelecatic left lung was less than half that of the ventilated right lung. When intravascular pressure is decreased by hemorrhage in the presence of regional atelecasis, Q/A increases due to a disproportionate increase in pulmonary vascular resistance in the ventilated lung, so that flow is increased to the ventilated lung and is maintained in the atelecatic lung.5 With nitroprusside, however, it appears that vascular resistance decreases in the atelecatic lung and is unchanged in the ventilated lung. Thus, it appears that hemorrhage and nitroprusside increase Q/A in this model by two different mechanisms. It is likely that any procedure or drug causing pulmonary hypotension will increase Q/A in this model of regional atelecasis, but the mechanisms may differ.

The results of this study suggest that when regional atelecasis is present nitroprusside can cause marked decreases in PaO2 and increases in Q/A. When nitroprusside is administered to patients who have substantial ventilation-perfusion abnormalities and atelecasis, a high inspired concentration of oxygen should be used, and arterial blood-gas values should be monitored.

References


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