Sodium Nitroprusside As An Adjunct To Pediatric Perfusion

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ABSTRACT

Sodium nitroprusside (N) has been administered to pediatric patients undergoing cardiopulmonary bypass with hypothermia for surgical repair of congenital heart defects. The rationale is to limit peripheral constriction due to cooling while maintaining a high flow perfusion (3.0 to 3.5 L/min/m²). Patients ranging in size from 4.0 to 33.6 kg (18.2 mean) and in age from 0.25 to 15 years (6.9 mean) have been treated during the past year. While the patients were being cooled to 23°C on pump, N (50 mg/500 cc) was administered into the arterial reservoir of the oxygenator with a minidrip set connected to an infusion pump. Rate of infusion was 2.5 to 10.8 µgm/kg/min (5.4 µgm/kg mean). The mean arterial pressure was maintained at 40 to 50 mmHg. Once the patients were at 23°C, N infusion was discontinued. Hypothermic potassium arrest of the heart was used in conjunction with this technique following aortic cross-clamping. N was administered again during rewarming at a slightly higher rate of infusion than when cooling. Advantages of the technique are increased tissue perfusion as evidenced by increased urine output on bypass, decreased fluid replacement in the postoperative period, and uniform body cooling/rewarming.

INTRODUCTION

Sodium nitroprusside (N) is a potent vasodilator that has gained increased usage in recent years primarily to treat patients with left ventricular dysfunction.¹,² Its action lowers mean arterial pressure by directly relaxing vascular smooth muscle. In doing so, peripheral resistance is lowered and left ventricular preload is lowered. It also decreases right atrial pressure secondary to dilation of peripheral capacitance vessels and decreases pulmonary artery pressure by directly dilating the pulmonary vasculature.³

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TABLE I

<table>
<thead>
<tr>
<th>Wt. kg</th>
<th>BSA m²</th>
<th>Procedure</th>
<th>Hypothermia</th>
<th>Flow L/min/m²</th>
</tr>
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<tbody>
<tr>
<td>12.0</td>
<td>.55</td>
<td>Closure VSD</td>
<td>24°</td>
<td>2.80</td>
</tr>
<tr>
<td>33.6</td>
<td>1.22</td>
<td>Rep.Dbl.Out.L V</td>
<td>23°</td>
<td>2.80</td>
</tr>
<tr>
<td>12.4</td>
<td>.59</td>
<td>Rep.A-V Canal</td>
<td>24°</td>
<td>2.90</td>
</tr>
<tr>
<td>26.0</td>
<td>.90</td>
<td>Rep.A-V Canal</td>
<td>23°</td>
<td>2.40</td>
</tr>
<tr>
<td>14.5</td>
<td>.67</td>
<td>Rep. Tetralogy</td>
<td>23°</td>
<td>2.75</td>
</tr>
<tr>
<td>23.0</td>
<td>.88</td>
<td>Rep.A-V Canal</td>
<td>26°</td>
<td>3.30</td>
</tr>
<tr>
<td>15.0</td>
<td>.67</td>
<td>Closure VSD</td>
<td>23°</td>
<td>3.25</td>
</tr>
<tr>
<td>12.4</td>
<td>.54</td>
<td>Rep. Tetralogy</td>
<td>23°</td>
<td>2.80</td>
</tr>
<tr>
<td>29.5</td>
<td>1.11</td>
<td>Closure VSD</td>
<td>23°</td>
<td>2.60</td>
</tr>
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<td>4.0</td>
<td>.24</td>
<td>Closure VSD</td>
<td>23°</td>
<td>3.55</td>
</tr>
<tr>
<td>Mean</td>
<td>18.2</td>
<td>.74</td>
<td>23.5°</td>
<td>2.92</td>
</tr>
<tr>
<td>±SEM</td>
<td>2.9</td>
<td>.09</td>
<td>.3</td>
<td>.11</td>
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Use of N during general anesthesia and surgery has been reviewed by Tinker. Advantages of N over the other common vasodilator, chlorpromazine, are twofold: 1) with N, there is a rapid return to normal blood pressure values following its discontinuation, and 2) there is little tachyphylaxis. With chlorpromazine, the duration of vasodilation often becomes disproportionately longer with increased dosages. Furthermore, N can be used during cardiopulmonary bypass to control hypertension rapidly. No acidosis has been reported with this mode of use.

Lappas and coworkers evaluated the hemodynamic response to N administration in coronary artery bypass graft patients and found substantial hemodynamic improvement in those with left ventricular dysfunction following surgery. Benzing and coworkers used N on pediatric patients in the postcardiopulmonary bypass period for low cardiac output states when the systemic vascular resistance was elevated. They observed that following hypothermic perfusion to 20°C, the patient’s vascular resistance was often increased. Another advantage noted with N therapy in their group of patients was an 81% increased urine output compared with patients who did not receive N.

The purpose of this paper is to present a technique for N administration during cardiopulmonary bypass with pediatric patients undergoing surgical correction of congenital cardiac defects. Data from ten patients are presented detailing dosages used, urine output and fluid replacement on pump, and cooling and rewarming times. Clinical observations and possible mechanisms for the advantages of N therapy during cardiopulmonary bypass will be discussed.

MATERIALS AND METHODS

The patient population is shown in Table I. All patients had hypothermic, isotonic potassium cardioplegic solution infused into the heart following aortic cross-clamping to provide myocardial protection and a flaccid, dry operative site. Patients were cooled systemically to an average temperature of 23.5°C (±.3 SEM) measured both tympanically and rectally. Rationale for using hypothermia was to decrease the temperature gradient between the arrested cold heart (15–20°C) and the systemic circulation. Secondly, by decreasing the patient’s temperature the oxygen requirements were decreased.
allowing a decrease in blood flow rate if needed to provide a dry operative field. Average weight of the patients was 18.2 kg (±2.9 SEM) and average body surface area was .74 m² (±.09 SEM). Average blood flow rate was 2.92 L/min/m² (±.11 SEM).

N administration was precisely and simply controlled by using an IVAC infusion pump* connected to a minidrip administration set. The minidrip was connected to an infusion port on the bubble oxygenator**. By using 50 mg of N in a 500 cc bag of Dextrose 5%/water, the following information was calculated:

1 cc = 0.1 mg or 100 μgm

and

1 cc = 60 drops (minidrip set)
then

1 drop = 1.67 μgm

Anesthesia consisted of ketamine induction followed by halothane for maintenance, and pancuronium was used as a muscle relaxant.

Cooling and N administration were begun immediately after establishing cardiopulmonary bypass at a calculated flow of 3.0 L/min/m². The amount of N given was dependent upon the hemodynamic response of each patient rather than by a strict protocol. Average dosage during cooling was 5.37 μgm/kg/min (±.67 SEM). The mean arterial pressure was lowered to 40 to 50 mmHg and maintained at this level until the patient’s temperature was 23°C. Blood flow rate was maintained at 3.0 L/min/m² during cooling. Once the patient was cooled, N administration was discontinued, and, depending on the amount of blood in the operative site, blood flow rate was decreased to 2.5 L/min/m². Hypothermic isotonic potassium arrest of the heart was accomplished by infusion of cardioplegic solution (25 mEq/L) with a roller pump through an infant bubble trap*** where both temperature and infusion pressure were monitored.6 Cardioplegic solution temperature averaged 13.3°C (±0.4 SEM) and the amount infused averaged 867 (±17 SEM). Intramyocardial temperature was monitored by means of a needle temperature probe**** placed directly into the free left ventricular wall. The hearts were cooled to 15.4°C (±0.6 SEM). Duration of aortic crossclamp averaged 36 minutes (±6 SEM). Additional cardioplegic solution was reinfused if the myocardial temperature drifted above 20°–22°C. Rewarming of the patient was begun at time of crossclamp removal. Simultaneously, N administration was reinitiated. Dosages during rewarming were slightly higher than those used during cooling and averaged 6.72 μgm/kg/min (±1.05 SEM). Blood flow rate was increased to 3.0 to 3.5 L/min/m² to compensate for increased oxygen demand and to facilitate rewarming. Water-to-blood temperature gradient was 8° to 10°C., and water temperature never exceeded 42°C. Just prior to terminating bypass, N infusion was stopped. Cardiopulmonary bypass was discontinued when the patient’s temperature reached 35° rectally and 38° tympanically.

* IVAC Corp., San Diego, Ca., Model 530.
** Cobe Laboratories Inc., Lakewood, Co., Model 42-201.
**** YSI Inc., Yellow Springs, Ohio, Model 524.
RESULTS

All patients tolerated N administration during the cooling and rewarming phases of cardiopulmonary bypass well, and there were no complications related to its use. Total dosages of N are shown in Table II. N administration varied due to differences in patient weight and duration of infusion but averaged .27 mg/kg (±.04 SEM). This is substantially less than the 3.0–3.5 mg/kg toxic dose cited by Tinker. Urine output on pump averaged 3.61 cc/min/m² (±.79 SEM), and fluid balance immediately following bypass averaged 12.7 cc/min/m² (±2.51 SEM). Average cooling time was 17.0 minutes (±1.5 SEM), and average rewarming time was 26.5 minutes (±1.5 SEM). In the immediate post bypass period there was no temperature drift as shown in a typical temperature curve in Fig. 1.

Hemodynamically, the patients required little additional fluid other than for maintenance or replacement for chest tube drainage. They arrived in the intensive care unit with no signs of peripheral vasoconstriction and with warm extremities. Acid-base balance remained in the normal range without the addition of sodium bicarbonate.

DISCUSSION

Use of N during cardiopulmonary bypass with hypothermia has been found to be an ideal time to use vasodilator therapy. Volume management is controlled easily by adding fluid to the extracorporeal circuit. Cardiac output or total blood flow is controlled by pump speed. Use of a minidrip administration set in conjunction with an infusion pump allows precise dosages to be administered over a wide range of values. The infusion pump has an alarm to notify the perfusionist if the proper amount of drug administration is not being maintained due to mechanical problems. This allows the perfusionist to concentrate on management of the perfusion without undue distraction.

Some patients have been reported resistant to the effects of N and may require a larger than predicted dose in order to lower their mean arterial pressure. None of the patients in this series showed evidence of this but caution should be exercised when using

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**TABLE II**

Nitroprusside Dosages n = 10

<table>
<thead>
<tr>
<th>Wt.kg</th>
<th>Cooling</th>
<th>Rewarming</th>
<th>Total N</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>μgm/kg/min</td>
<td>μgm/kg/min</td>
<td>μgm/kg</td>
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<tr>
<td>12.0</td>
<td>6.96</td>
<td>4.17</td>
<td>2250.19</td>
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<td>33.6</td>
<td>2.74</td>
<td>2.49</td>
<td>3900.12</td>
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<td>12.4</td>
<td>6.73</td>
<td>8.06</td>
<td>4400.35</td>
</tr>
<tr>
<td>26.0</td>
<td>5.12</td>
<td>3.85</td>
<td>5100.20</td>
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<tr>
<td>14.5</td>
<td>3.45</td>
<td>6.90</td>
<td>2500.17</td>
</tr>
<tr>
<td>23.0</td>
<td>2.54</td>
<td>2.54</td>
<td>2050.09</td>
</tr>
<tr>
<td>15.0</td>
<td>5.00</td>
<td>10.50</td>
<td>6000.40</td>
</tr>
<tr>
<td>12.4</td>
<td>9.44</td>
<td>10.80</td>
<td>4100.33</td>
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<td>29.5</td>
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<td>13,700.46</td>
</tr>
<tr>
<td>4.0</td>
<td>5.50</td>
<td>10.75</td>
<td>1650.41</td>
</tr>
<tr>
<td>Mean 18.2</td>
<td>5.37</td>
<td>6.72</td>
<td>1650.41</td>
</tr>
<tr>
<td>±SEM 2.9</td>
<td>.67</td>
<td>1.05</td>
<td>.04</td>
</tr>
</tbody>
</table>
Pt. wt. 26.0 kg
Procedure: Repair A - V Canal

![chart](chart.png)

Figure 1. A typical temperature plot showing a patient's tympanic temperature during surgery and rectal temperature in the ICU immediately postoperatively. Note lack of temperature drift in the post bypass period.

this technique. If excessively large dosages of N are given, the possibility of patients developing cyanide toxicity should be considered.

Normal vascular response to hypothermia depends on the temperature. As temperature decreases to approximately 28°C, there is a slight vasoconstriction as the body attempts to regulate blood flow away from the periphery to vital organs. However, below 26°–28° the body regulatory mechanisms are inactive and vasodilation usually occurs. The advantage of N appears to be in overcoming the initial vasoconstriction. Instead of shunting and non-uniform cooling, use of N allows a more uniform distribution of cold blood, and the organism is cooled uniformly. Although uniform body cooling/rewarming is difficult to measure in the clinical setting, the fact that N treated patients presented in this series arrived in the intensive care unit with warm extremities would indicate that the rewarming process was uniform. No evidence of organ dysfunction related to poor perfusion developed in any patient. Also, the fact that the acid-base status remained essentially unchanged with no metabolic acidosis occurring would indicate good tissue perfusion at every level.

Some of the factors that have been observed in experimental animals subjected to hypothermia leading to poor tissue perfusion are: 1) increased blood viscosity, 2) pooling of blood in capillaries and venules, 3) development of red blood cell aggregates, 4) arteriolar constriction, and 5) development of A-V shunting. N by its vasodilatory effect would
appear to counteract several of these phenomena. Of course, use of heparin and hemo-
dilution as requisites of cardiopulmonary bypass are also advantageous in preventing
poor tissue perfusion.

Garber has reported results of a study using dogs undergoing hypothermic perfusion
at constant flow rates. During the cooling phase there was a gradual uptake of fluid from
the arterial reservoir and upon rewarming the opposite was true. This was not observed
in our experience which may be related to use of N. The possible mechanism would be
prevention of A-V shunting and capillary pooling of the perfusate.

CONCLUSIONS

N has been found to be a useful and safe adjunct to hypothermic perfusion of pe-
diatric patients. Caution needs to be exercised regarding infusion rate so that hypotension
and cyanide toxicity are avoided.

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