Inhaled Nitric Oxide Improves Hepatic Tissue Oxygenation in Right Ventricular Failure: Value of Hepatic Venous Oxygen Saturation Monitoring

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NITRIC oxide inhalation has been shown to have therapeutic benefits through its action as a selective pulmonary vasodilator. In a number of conditions in which pulmonary hypertension was prominent, nitric oxide inhalation reduced pulmonary artery pressures and improved arterial oxygenation.1-4 As the right ventricle (RV) normally ejects against a low impedance circulation, reduction of a pathologically increased RV afterload can be anticipated to be beneficial. Therefore, in the presence of an impaired myocardial contractile function, the reduction of even a modestly increased RV afterload also may be therapeutic.

We report the case of a patient with severe cardiomyopathy, mild pulmonary hypertension, and severe congestive hepatic failure, in whom nitric oxide inhalation decreased RV afterload and led to a rapid relief of visceral congestion. This was assessed by continuous monitoring of hepatic venous oxygen saturation demonstrating an improvement in the hepatic oxygen delivery:consumption ratio.

Case Report

A 38-yr-old man consulted his doctor because of tiredness and shortness of breath on exertion. On clinical examination, he appeared to be in congestive cardiac failure, and given the rapid evolution of his symptoms, the patient was urgently referred to our hospital.

On admission to the intensive care unit for the management of his cardiac failure, his temperature was 35.5°C, heart rate 140 beats/min, and arterial blood pressure 110/80 (91) mmHg. Physical examination found signs of a predominantly right-sided congestive cardiac failure with full jugular veins and tender hepatomegaly. The patient's respiratory rate was 30 breaths/min, and no pulmonary abnormalities were noted on auscultation. The electrocardiogram revealed atrial fibrillation and a right bundle branch block. A chest x-ray did not show pulmonary edema, and the cardiothoracic ratio was 0.63. Pulse oximetry while breathing oxygen (6 l/min) via nasal prongs showed a 95% oxyhemoglobin saturation (Svo2). Urine output ranged from 10 to 25 ml/h.

The initial blood tests indicated a hepatocellular and renal dysfunction: aspartate aminotransferase (AST) 9,940 IU/l (normal < 35), alanine aminotransferase (ALT) 5,260 IU/l (normal < 56), total bilirubin 37 μmol/l (normal < 17), factor II 57%, factor V 12%, fibrinogen 1.2 g/l (normal 2-4), albumin 33 g/l (normal > 39), urea 13 mm (normal < 5), and creatinine 230 μmol (normal < 110). A partially compensated metabolic acidosis was present: pH 7.34, Pco2 32 mmHg, bicarbonate 17 mm, lactate 5.4 mm (normal < 2.0). Hemoglobin was 11.3 g/dl, and leukocyte count 11,000/mm3. A complete viral serology screen was negative.

Echocardiography showed both ventricles to be dilated and hypokinetic, and the inferior vena cava was dilated: RV end-diastolic diameter measured 50 mm, left ventricular (LV) end-diastolic diameter 70 mm, LV shortening fraction < 15%, and inferior vena cava diameter 26 mm. However, as Doppler studies were not available, valve competency could not be evaluated. Abdominal ultrasound scan revealed an enlarged and homogenous liver measuring 20 cm in the midclavicular line.

Hemodynamic measurements obtained via a fiberoptic flow-directed pulmonary artery catheter (Opticath model P7110-EH, Oximex, Mountain View, CA) confirmed the left and right ventricular dysfunction: right atrial pressure (RAP) 29 mmHg, pulmonary artery pressures (PAP) 55/44 (49) mmHg, pulmonary artery wedge pressure 32 mmHg, and cardiac output 4.0 l/min, with a stroke volume of 26 ml and mixed venous oxygen saturation Sv02 47%.

Given the severity of hepatic dysfunction, our treatment strategy was targeted at improving hepatic oxygenation. We chose the hepatic venous oxygen saturation as a rapid and useful parameter to assess the hepatic oxygen delivery/consumption balance. A second fiberoptic pulmonary catheter was inserted into a hepatic vein via the right internal jugular vein, and the position was verified echographically. The mean hepatic venous pressure (Pvh) was 31 mmHg, and

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there was no gradient with hepatic wedged pressure. Hepatic venous
blood was withdrawn from the distal port of the catheter, and hepatic
venous oxygen tension (PhvO₂) was 18 mmHg (ABL30, Radiometer,
Copenhagen). The measured hepatic venous oxygen saturation
(ShvO₂) was 20% at this time.

We hypothesized that the impaired hepatic oxygenation was due
to congestion of the liver rather than to systemic hypoperfusion. To
reduce hepatic congestion, we set up a continuous arteriovenous
hemofiltration (AN695, Hospal, France) to remove fluid. After 12 h
of continuous arteriovenous hemofiltration, a net fluid loss of 2,300
ml was achieved. Although this brought about a reduction in RAP
(from 29 to 17 mmHg) and an increase in ShvO₂, (from 20% to 35%),
the hepatic enzyme activity was unchanged as compared to the values
obtained on intensive care unit admission. An additional infusion of
15 g/h dextrose also became necessary to maintain normoglycemia.

At this time, the patient began to show signs of respiratory muscle
fatigue; respiratory rate increased from 25/min to 40/min, and arterial
carbon dioxide tension (PaCO₂) increased from 30 to 45 mmHg. He
required orotracheal intubation and mechanical ventilation (zero
positive end-expiratory pressure and Fio₂, 1.0) after which an im-
mEDIATE increase in SvO₂ was observed. The ShvO₂, however, decreased
abruptly to unrecordable levels, and a hepatic venous sample drawn
during this time found a PhvO₂ of 12 mmHg.

Initiation of mechanical ventilation also increased the Phv, indi-
cating a worsening of RV function, probably because of a critical
increase in RV afterload (increased mean pulmonary artery pressure,
PAPm, from 34 to 44 mmHg). This would have exacerbated hepatic
congestion and further impaired hepatic tissue oxygenation. We
reasoned that, by using inhaled nitric oxide to reduce right ventricular
afterload, we could improve the failing RV function and relieve he-
patic congestion. We administered nitric oxide continuously at a
dose of 18 ppm (by volume) to an intratracheal catheter as previ-
ously described. Within 10 min of nitric oxide inhalation, we ob-
served a decrease in pulmonary artery pressures (PAPm from 44 to
30 mmHg), RAP (from 22 to 19 mmHg), and Phv (from 24 to 20
mmHg). Increases in both stroke volume (from 22 to 27 ml) and
mean arterial pressure (from 88 to 96 mmHg) were noted. The pul-
monary artery wedge pressure could not be determined because the
catheter failed to wedge, but the pulmonary artery diastolic pressure
(PADp) decreased slightly from 38 to 35 mmHg (table 1). Both
SvO₂ and ShvO₂ increased dramatically, and we noted a transient in-
crease of ShvO₂ above SvO₂ (fig. 1). A repeat echocardiographic
examination showed no change in LV diameters, but the RV could not
be totally visualized. The diameter of the inferior vena cava decreased
from 26 to 20 mm.

Hepatic enzyme activity decreased after nitric oxide was admin-
istered: AST 1,460 and ALT 1,760 at 12 h of nitric oxide inhalation,
and AST 290 and ALT 1,460 IU/L at 48 h of nitric oxide inhalation.
ShvO₂ was stable at about 72% (PhvO₂ 43 mmHg). Inhaled nitric oxide
was given continuously for 5 days with no apparent side effects,
and the methemoglobin level measured daily was less than 1.3%. Hepatic
enzyme activity within our reference laboratory range was noted 7
days after the start of nitric oxide inhalation. The patient remained
in the intensive care unit for a further 3 weeks because of a Strep-
tococcal pulmonary infection, and he was discharged home 7 weeks
after hospital admission.

Table 1. Hemodynamic and Metabolic Parameters after 12
Hours of Continuous Arteriovenous Hemofiltration (CAVH),
and Initiating Mechanical Ventilation without Nitric Oxide
(NO) Inhalation and 30 Minutes after Continuous Inhalation
of NO

<table>
<thead>
<tr>
<th>Spontaneous Ventilation</th>
<th>Mechanical Ventilation before NO</th>
<th>Mechanical Ventilation 30 min after NO</th>
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</thead>
<tbody>
<tr>
<td>12 h after CAVH</td>
<td>160</td>
<td>154</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>150</td>
<td>160</td>
</tr>
<tr>
<td>RAP (mmHg)</td>
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<td>22</td>
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<tr>
<td>Phv (mmHg)</td>
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<td>PAP (mmHg)</td>
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<td>PAPm (mmHg)</td>
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<td>PAPm (mmHg)</td>
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<td>MAP (mmHg)</td>
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<tr>
<td>CO (L/min)</td>
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<td>SV (ml)</td>
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<td>SvO₂ (%)</td>
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</tr>
<tr>
<td>ShvO₂ (%)</td>
<td>35</td>
<td>12</td>
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</tbody>
</table>

HR = heart rate; RAP = right atrial pressure; Phv = mean hepatic venous pressure; PAP, PAPm, PAPs = pulmonary artery pressure: systolic, diastolic,
and mean respectively; MAP = mean arterial pressure; CO = cardiac output;
SV = stroke volume; Pao₂, Paco₂, PhO₂ = arterial, mixed venous, and hepatic
venous oxygen tension, respectively; StpO₂ = oxyhemoglobin saturation by pulse
oximetry; SvO₂, ShvO₂ = mixed venous and hepatic venous oxygen saturation,
respectively. During mechanical ventilation, blood gas values are measured on
FeO₂ 1.0.

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Discussion

The combination of increased liver enzymes and a low Shvo₂ at 20% indicated a severe hepatic ischemia. Hepatic ischemia may result, in theory, from a reduction in cardiac output that reduces liver blood flow. Alternatively, a high hepatic venous back pressure may decrease hepatic perfusion pressure and consequently reduce liver blood flow. Our patient’s cardiac output (4.0 l/min) should have ensured an adequate hepatic blood flow, and it is likely that, in this case, hepatic ischemia resulted from the increased hepatic back pressure. This was supported by clinical data compatible with hepatic congestion: increased liver size, dilated inferior vena cava, and increased hepatic venous pressure. The improved hepatic oxygenation that followed Phv decrease after nitric oxide inhalation is also in favor of hepatic congestion.

The rapid decrease in hepatic venous pressure was unlikely to be a systemic effect of nitric oxide, because inhaled nitric oxide diffuses across the alveolar membrane into the intravascular space and is rapidly inactivated by hemoglobin. Furthermore, in our patient, neither systemic vasodilation nor hypotension was observed after nitric oxide administration. The most probable mechanism of the decrease in Phv was, therefore, a reduction in the afterload of a failing right ventricle as suggested by the decrease in PAP values; this led to an improvement in the function of the failing RV and a decrease in peripheral venous pressure. A similar mechanism has been observed with other pulmonary vasodilators, including prostacyclin.

Our report also shows a dramatic improvement in Shvo₂ soon after nitric oxide inhalation (fig. 1). The Shvo₂ signal moved from an undetectable level to greater than the mixed venous oxygen saturation value. Shvo₂ then remained stable at an adequate level. Because none of the techniques or drugs used in this patient’s treatment are known to reduce hepatic oxygen consumption, we might assume that the improved hepatic oxygenation was a result of increased hepatic oxygen delivery after the slight increase in cardiac output. However, perhaps a more important factor was the reduction in hepatic venous pressure after nitric oxide inhalation and the resultant increase in hepatic perfusion pressure. The modest decrease in hepatic venous pressure had a substantial effect on hepatic oxygenation. The Shvo₂ was observed to exceed the Svvo₂ transiently. This may represent a preferential liver perfusion, as has been described in posts ischemic reperfusion, or intrahepatic shunting.

In summary, inhaled nitric oxide was able to improve impaired RV function by selectively reducing RV afterload. This led to the relief of hepatic congestion, improved hepatic tissue oxygenation, and halted the progression of hepatocellular damage. Inhaled nitric oxide should be considered as an effective treatment of visceral congestion due to RV dysfunction, even in the presence of modest pulmonary hypertension. We showed that continuous monitoring of hepatic venous oxygen saturation was useful for assessing hepatic oxygen balance and for monitoring the effects of treatment.

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References


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