Reduction of Plasma Nitric Oxide in a Patient with Endotoxic Shock by Hemoadsorption Therapy

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Endotoxin, pg/ml Nitric oxide, $\mu\text{mol/l}$ Endothelin, pg/ml Cyclic GMP, pmol/ml

Dear Sir,

Patients with septic shock due to gram-negative bacillus infections have been reported to have endotoxemia. Endotoxin has been reported to produce nitric oxide in endothelial cells [1]. Nitric oxide is a powerful vasodilator and causes severe hypotension in patients with endotoxemia [2]. We describe the effects of hemoadsorption on endotoxemia and plasma nitric oxide levels in a 72-year-old man with septic shock.

The patient had been undergoing hemodialysis of acute renal failure due to rhabdo-myolysis. Although renal function had recovered after 5 weeks of hemodialysis, the patient had septic shock due to a large decubitus infection. He was suffering from high fever and acute hypotension (blood pressure 90/40 mm Hg). Laboratory investigations disclosed: white blood cells $13,890/\text{mm}^3$; C-reactive protein 13.7 mg/dl ; blood urea nitrogen 84.7 mg/dl , and creatinine 4.5 mg/dl . The plasma endotoxin concentration was 13.5 pg/ml (normal $< 5 \text{ pg/ml}$) by specific chromogenic limulus test, and the plasma nitric oxide level was $146 \mu\text{mol/l}$ (normal range $10\text{--}71 \mu\text{mol/l}$) by HPLC. Plasma endothelin was 10.1 pg/ml (normal range $< 2.0 \text{ pg/ml}$) and plasma cyclic GMP was 2.0 pmol/ml (normal range $1.8\text{--}4.8 \text{ pmol/ml}$) by radioimmunoassay. Methicillin-resistant Staphylococcus aureus was detected in blood cultures. Methicillin-resistant S. aureus has been reported to produce toxic shock syndrome toxin-1. It is well known that endotoxin is reinforced with toxic shock syndrome toxin-1 in vivo [3,4]. We performed hemoadsorption using a polymyxin B immobilized fiber column (PMX-20R Toraymyxin, Toray Medical Co, Tokyo, Japan) with direct hemoperfusion for 2 h. Blood pressure was restored ($140/50 \text{ mm Hg}$) and the elevated plasma concentrations of endotoxin, nitric oxide, endothelin and cyclic GMP were all reduced by

hemoadsorption (table 1). The nitric oxide level decreased to 56% of the pre-adsorption level. On the other hand, the decrease in the plasma endothelin level was moderate (28%) after hemoadsorption.

Septic or endotoxic shock is associated with high mortality and morbidity rates. In patients with septic shock, high plasma nitric oxide levels are well correlated with high plasma endotoxin levels and low systemic vascular resistance [5]. Endotoxin stimulates macrophages to release cytokines including interleukin-1, tumor necrosis factor and platelet-activating factor. These cytokines stimulate vascular endothelial cells to release a variety of vasoconstrictors such as endothelin or thromboxane as well as vasodilators such as nitric oxide or prostacyclin [5]. The balance of vasoconstrictors and vasodilators is altered in many pathological conditions [6]. Increased nitric oxide in septic shock may stimulate an increase in cyclic GMP, resulting in decreased vascular resistance. After elimination of endotoxin by hemoadsorption, the altered balance may have been normalized in the present case. The vascular resistance was increased, and consequently systemic blood pressure was restored. Petros et al. [7] demonstrated that NG-L-monomethyl arginine and NG-nitro-L-arginine methylester, both nitric oxide syn-thase inhibitors, were effective in the treatment of patients with endotoxic shock.

These results suggest that hemoadsorption therapy may be useful for removing endotoxin from the circulation of patients with endotoxic shock.

Table 1. Laboratory data before and after hemoadsorption
Hemoadsorption

before

after

13.5

< 3.0

146

64

10.1

7.1

2.0

0.3

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