症 例

Disparate Hemodynamic Responses to Injections of Methylprednisolone in a Septic Shock Patient with Long-term Catecholamine Administration

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Introduction

Septic shock patients are usually given large doses of exogenous catecholamines to maintain the hemodynamic state. However, long-term catecholamine administration induces resistance to catecholamine presumably due to decreases in the β-adrenergic receptors which is called "down-regulation of β-receptors"[1~12]. This is commonly due to disturbance of the adenylate cyclase system. On the other hand, several investigations have showed that large doses of steroid hormones are able to improve the deterio-rated hemodynamics in septic shock patients[4~12].

We observed a marked improvement in blood pressure by a different mechanism after administration of 2000 mg methylprednisolone in a septic shock patient under long-term treatment with catechol-amine.

Case Report

The patient was a 43-year-old, 48-kg, 161-cm male. He had undergone a pancreaticoduodenectomy after diagnosis of chronic alchoholic pancreatitis in October 18, 1983. In July 24, 1992, he was transferred to our hospital because of febrility, anemia, and drowsiness which had appeared several days before.

He was diagnosed with a liver abscess by abdominal echo and computed tomographic(CT)scan. In spite of intravenous injections of broad-spectrum antibi-otics and drainage of the source of infection, he showed signs of septic shock. Finally, he was placed in the ICU on July 28, 1992.

After admission to the ICU, the patient remained somnolent, and continuous infusions of $5\,\mu g \cdot kg^{-1} \cdot min^{-1}$ of dopamine and $0.4\,\mu g \cdot kg^{-1} \cdot min^{-1}$ of norepinephrine were required to maintain the blood pressure with in the normal range. On the 9th day of ICU admission, however, despite of continuous $10\,\mu g \cdot kg^{-1} \cdot min^{-1}$ of dopamine and $0.8\,\mu g \cdot kg^{-1} \cdot min^{-1}$ of norepinephrine infusion, systolic and diastolic BP decreased to 90 and 50 mmHg, respectively. On suspicion of down-regulation or desensitization of β-adrenergic receptors by the prolonged catecholamine treatment, we injected 2000 mg of methylprednisolone. From one hour after the injection, BP began to recover gradually, and after 12 hours, it was possible to decrease the doses of dopamine and norepinephrine to 3 and $0.2\,\mu g \cdot kg^{-1} \cdot min^{-1}$, respectively. Systemic BP improved to 130/60 mmHg and pulse pressure to 70 mmHg. In comparison with the hemodynamics before injection of methylprednisolone, cardiac output and heart rate increased from 5.54 to 9.80 $L \cdot min^{-1}$ and from 60 to 130 $beats \cdot min^{-1}$, respectively, and systemic vascular resistance decreased from 664 to 400 $dyne \cdot sec \cdot cm^{-5}$. But after twenty hours, this hemodynamic state began to relapse, and forty hours later, the patient required the same doses of catecholamines which had been infused before administration of methylprednisolone.

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Over a few days after this episode, he remained at a systolic BP of about 100 mmHg with continuous 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of dopamine and 0.8 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of norepinephrine infusion. However, on the 20th day after the first injection of methylprednisolone, we had to inject 2000 mg of methylprednisolone again. BP recovered dramatically just as it had after the first injection; an hour later it was 120/70 mmHg and 6 hours later was still over 110/60 mmHg despite continuous infusions of smaller dose of 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of dopamine and 0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of norepinephrine.

However, the hemodynamic responses were different from that after first injection of methylprednisolone (Table 1); the pulse pressure and heart rate did not increase, cardiac output fell slightly, and systemic vascular resistance increased from 369 to 674 dyne·sec·cm^{-5} so that right and left ventricular stroke work in creased from 5.7 to 22.5 g·m and from 109 to 171 g·m, respectively. The above parameters remained at their altered values for about 48 hours and hemodynamic variables were also stable for about 3 days. On the 4th day after the 2nd injection, the patient fell into severe hypotension, renal and respiratory failure, and on the 49th hospital day, he died of severe hypoxemia.

Discussion

The mechanisms of the elevation of blood pressure by steroid hormones are thought to be involved with an increase of cardiac output or systemic vascular resistance.

1) Cardiac output is increased by the recovery of myocardial β-adrenergic receptor responsiveness, number, or function[4~12].

2) Systemic vascular resistance increases due to the simultaneous constriction of smooth muscle of peripheral vessels[13,14].

We performed two intravenous injections of large doses of methylprednisolone in a patient. After both, his blood pressure increased but the hemodynamic responses after the first and the second injections differed. After the first injection, heart rate increased, systemic vascular resistance decreased and cardiac output remarkably increased, which indicate that the hemodynamic changes were caused by the stimulation of myocardial β-adrenergic receptors; several investigators have reported such stimulation. On the other hand, after the second injection, heart rate tended to decrease and the cardiac output remained approximately constant, while the BP rose with systemic vascular resistance. The latter hemodynamic changes had nothing to do with stimulation of β-adrenergic receptors. These findings suggest that steroid hormones result in disparate responses on hemodynamics in a septic shock patient after long-term catecholamine administration.

Besse et al.[13] and Kalsner et al.[14] showed that steroid hormones enhanced vascular response to catecholamine stimulation. Wilson et al. reported that in a state of septic shock leading to an increasing cardiac output and decreasing vasomotor tone,

Table 1. Changes of hemodynamic parameter values before and after MP injection

	parameter			
	CO (L/min)	HR (beats/min)	BP (mmHg)	SVR (dyne·sec/cm^5)
19 th day after ICU admission				
before injection	5.54	60	90/50	664
1 hour after injection	9.80	130	130/60	400
40 th day after ICU admission				
before injection	11.90	86	99/57	369
1 hour after injection	11.00	80	120/70	674

MP, methylprednisolone; CO, cardiac output; HR, heart rate;
SVR, systemic vascular resistance

steroid hormones contributed to an increase in systemic vascular resistance and the normalization of cardiac output[15]. Those reports and our results suggest that steroid hormones act to enhance the vascular responsiveness and tonus of peripheral vessels.

Steroids have received some attention of late for their inhibition of generation of nitric oxide(NO)[16,17].

It is possible that NO acted in the present case to decrease systemic vascular resistance after induction by endotoxin and/or cytokines. Actually as shown in Table 1, the SVR before the second methylprednisolone administration was much lower as compared with that bofore the first administration. This decreased SVR might have been caused by increased NO synthesis. If this is true, the mechanism of the blood pressure augmentation after the second injection of steroid hormones indicates recovery of systemic vascular resistance owing to inhibition of the generation of NO by steroids.

Recently, it has been reported that the expression, but not the activity, of NO synthase is inhibited by glucocorticoids[16~19]. NO synthase consists of two enzymes, one dependent and one independent of Ca^{2+}[16,17,20,21]. The Ca^{2+}-independent enzyme is inhibited by steroids[16,17,22] and is not induced over such short periods as typical in septic shock[21,23]. In this case, therefore, we speculate that Ca^{2+}-independent NO synthase was not induced at the first steroid injection. On the other hand, twenty days later at the second injection the NO synthesis was enhanced and the steroid administration inhibited it.

We observed two different hemodynamic responses in a patient after administration of 2000 mg methylprednisolone. The mechanisms of the elevation of blood pressure by methylprednisolone might invole activation of myocardial β-adrenergic receptors or that of peripheral vessels.

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(Circ Cont 18 : 84～87, 1997)