Pressor Response to Norepinephrine Infusion in Patients with Pheochromocytoma

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ABSTRACT

In a patient with pheochromocytoma, norepinephrine (NE) infusion test coupled with measurement of plasma NE concentration was performed. NE turnover rate was accelerated before the surgical removal of the tumor compared to post operation, but the pressor response showed no difference between the two.

INTRODUCTION

Because of the clinical difficulty in evaluating the vascular reactivity in hypertensive patients to NE directly, the pressor response to the amount of NE infused or the amount of NE required to obtain certain pressor response has been used for this purpose. By using these methods, decreased pressor response in pheochromocytoma and the improvement after surgical removal of the tumor have been reported. In these studies we performed the exogenous NE infusion test to a patient with the left adrenal pheochromocytoma with simultaneous measurement of blood pressure (BP) and plasma NE level, and compared them with the previous results determining BP alone.

MATERIALS AND METHODS

The pressor response to exogenous NE in a 40 year old female with a pheochromocytoma of left adrenal gland was studied before and after the surgical removal of the tumor.

Before the operation she was withdrawn from antihypertensive medication for 2 weeks prior to the study and allowed an unrestricted diet. She was then placed in a comfortable supine position under fasting conditions in the morning period. An indwelling venous catheter was placed in the antecubital vein in order to obtain blood samples without repeated venipuncture. Another catheter was placed in an instep vein for NE infusion. Blood pressure was monitored every minute by sphygmomanometric method, and heart rete was recorded by electrocardiogram. NE solution was prepared as 10 µg/kg/min in 5% glucose solution. After instrumentation the patient was kept in the supine position for an additional 30 min, and then a blood sample was obtained for plasma NE determination. NE infusion rate was started with 0.08 µg/kg/min with an infusion pump (Nihon Kohoden TFV 1100), and was increased in 0.04 to 0.10 µg/kg/min steps every 3 min until 1.20 µg/kg/min. Blood samples were also obtained at 0.08, 0.40, and 0.80 µg/kg/min NE infusion, respectively. NE was extracted from the deproteinized plasma by alumina, and was detected by electrochemical method by high performance liquid chromatography (Yanaco L-4000w).

The same study was repeated one week, 2 weeks, and 6 months after the operation.

RESULTS

1) Evaluation of pressor response by the previous method of NE infusion test

(Fig. 1) The blood pressure at the time of 6 months after the operation decreased significantly, compared with that prior to the operation.

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* 山本正治, 正岡智子, 金沢郁夫, 松浦秀夫, 須山健朗：褐色細胞腫におけるノルエピネフリン負荷時の血圧反応性
Table 1. The blood pressure and the plasma NE concentration before and during NE infusion

<table>
<thead>
<tr>
<th>NE Infusion Rate (µg/kg/min)</th>
<th>Before</th>
<th>0.08</th>
<th>0.40</th>
<th>0.80</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-ope P. NE</td>
<td>0.862</td>
<td>1.063</td>
<td>2.850</td>
<td>3.798</td>
</tr>
<tr>
<td>mBP</td>
<td>125</td>
<td>128</td>
<td>132</td>
<td>143</td>
</tr>
<tr>
<td>Post-ope 1 W P. NE</td>
<td>0.250</td>
<td>0.790</td>
<td>3.007</td>
<td>5.069</td>
</tr>
<tr>
<td>mBP</td>
<td>85</td>
<td>88</td>
<td>103</td>
<td>155</td>
</tr>
<tr>
<td>Post-ope 2W P. NE</td>
<td>0.142</td>
<td>0.830</td>
<td>3.610</td>
<td>6.245</td>
</tr>
<tr>
<td>mBP</td>
<td>104</td>
<td>110</td>
<td>133</td>
<td>142</td>
</tr>
<tr>
<td>Post-ope 6M P. NE</td>
<td>0.120</td>
<td>0.976</td>
<td>5.098</td>
<td>10.717</td>
</tr>
<tr>
<td>mBP</td>
<td>94</td>
<td>94</td>
<td>124</td>
<td>134</td>
</tr>
</tbody>
</table>

P. NE: Plasma Norepinephrine (ng/ml)  mBP: mean Blood Pressure (mmHg)

Fig. 1. The blood pressure responses to the exogenous NE before and 6 months after operation

Fig. 2. The shift of the dose response curve between m mean blood pressure and exogenous NE before, one week, two weeks, and 6 months after operation

before and during NE infusion. However, pressor response was observed from as little as 0.06 µg/kg/min of NE infusion rate postoperatively, whereas 0.30 µg/kg/min preoperatively. Fig. 2 shows the dose-response curve of mean blood pressure (\(\Delta mBP\)) to exogenous NE. The curve shifted to the left after the operation, which suggested the decreased pressor response to infused NE in pheochromocytoma and its improvement after the operation as reported previously.

2) Plasma NE concentration during exogenous NE infusion

Table 1 and Fig. 3 show plasma NE concentration before and during NE infusion. The basal plasma NE concentration before the operation was markedly elevated, compared with that prior to the operation (0.862 pre-ope, 0.250 post-ope 1W, 0.142 post-ope 2W, and 0.120 ng/ml post-ope 6M, respectively). There was a linear relationship between plasma NE concentration and logarithm of NE infusion rate,
It means that the pressor response to plasma NE, was not affected by the presence of pheochromocytoma and the previous method shown in Fig. 2 could not have evaluated the accurate pressor response to NE.

DISCUSSION

Decreased pressor response to exogenous NE in pheochromocytoma has been reported, and attributed to decreased vascular reactivity. Our findings that the dose-response curve shifted to the right before the operation became normal after the operation coincided with the previous reports. If the plasma NE concentration to the exogenous NE revealed an identical slope before and after the operation, the difference of pressor response between pre- and postoperation could have been well evaluated from the result above. In the present study, the plasma NE concentration increased linearly with the logarithm of NE infusion rate. However, the slope of line became steeper after the operation, as shown in Fig. 3. Therefore, the plasma NE concentration at a given NE infusion rate is different between the pre-operative period and 1 week and 2 weeks and 6 months after the operation, and it suggests the necessity of using pressure change coupled with plasma NE concentration in evaluating the pressor response to exogenous NE. These phenomena indicate that the turnover rate of exogenous NE is different between pre- and postoperation, suggesting the increased sympathetic neural uptake of NE or NE metabolism.

In pheochromocytoma the platelet α-adrenoceptor number decreased compared with normal subjects, which fact suggests the decrease in vascular reactivity which is incompatible with our results. The plasma volume, which is decreased before the operation, becomes normal after surgical correction. Some probable influence of a change in the plasma volume on pressor response cannot be denied. These problems should be clarified by further investigation.

Because of the clinical difficulty in evaluating vascular reactivity, we used pressor response. Mean blood pressure is regulated by cardiac output and systemic vascular resistance. Cardiac output hardly changes by exogenous NE infusion. Therefore, we consider that pressor response directly reflects changes in systemic vascular resistance, which is vascular reactivity,
and can be substituted for the latter.

The increased pressor response or vascular reactivity to infused NE has repeatedly been observed in hypertensive patients\textsuperscript{3,5,7,8}. However, such studies have not been coupled with specific measurement of plasma NE concentration. As we have shown in this study, pressor response should be evaluated by the pressure change against plasma NE concentration, and this should be considered in the evaluation of pressor response in hypertensive patients, too.

REFERENCES


