Circulating catecholamines and systolic time intervals in labile and sustained hypertension

D. COUSINEAU, J. DE CHAMPLAIN† AND L. LAPOINTE
Département de Physiologie, Faculté de Médecine, Université de Montréal, Montréal, Québec, Canada

Summary

1. Average supine circulating total catecholamine concentrations were found to be higher than the normal range in about 50% of patients with labile hypertension and in about 30% of patients with sustained essential hypertension.

2. These higher resting concentrations were mainly due to an increase in adrenaline in labile hypertension and to an increase in noradrenaline in sustained hypertension.

3. Patients with elevated catecholamine concentrations were also characterized by a higher heart rate, by an increased myocardial contractility and by greater hypotensive response after treatment with β-adrenoreceptor blocking agents.

4. These studies suggest the existence of subgroups of hypertensive patients with increased sympathetic tone.

Key words: catecholamines, hypertension, sympathetic tone.

Abbreviations: CA, catecholamine; NA, noradrenaline.

Introduction

Increased supine circulating catecholamine (CA) or noradrenaline (NA) concentrations have been reported in patients with essential hypertension (Engelman & Portnoy, 1970; de Quattro & Chan, 1972; Louis, Doyle & Anavekar, 1973; de Champlain, Farley, Cousineau & Van Ameringen, 1976; Lutold, Bühler & Da Prada, 1976; Reid, Jones & Dargie, 1977). Hypertensive patients with elevated circulating CA and NA concentrations were characterized by higher heart rate and lower pre-ejection period values as well as by a greater decrease in heart rate, myocardial contractility and blood pressure in response to treatment with β-adrenoreceptor blocking agents (de Champlain, Cousineau, Van Ameringen, Marc-Aurèle, Yamaguchi, 1977; Esler, Zweifler, Randall, Julius & de Quattro, 1977). Hypertensive patients with high resting concentrations of CA also respond to postural stimulation with greater increase in circulating CA or NA (Sever, Birch, Osikowska & Tunbridge, 1977; de Champlain et al., 1977) thus suggesting that the basal sympathetic tone and sympathetic reactivity may be higher in an important subgroup of hypertensive patients.

Systolic time intervals and circulating CA and NA concentrations were measured and adrenaline was estimated in normotensive subjects and in labile and sustained hypertension before and after propranolol treatment.

Methods

Twenty-eight normotensive subjects (13 males and 15 females) and 46 hypertensive patients (24 males and 22 females) were investigated between 13.00 hours and 14.00 hours. All medication was stopped for at least 3 weeks before the study. Labile hypertensive patients had recumbent blood pressure after 20 min below 150/90 mmHg but occasional casual blood pressures above that level whereas patients with recumbent blood pressure consistently above 150/90 mmHg were considered to have sustained hypertension.

After rest supine for 20 min, systolic time interval (pre-ejection period) was measured by simultaneous recording of the carotid pulse, phono-
# Table 1. Supine circulating catecholamine, noradrenaline and adrenaline concentrations in labile and sustained hypertension

<table>
<thead>
<tr>
<th></th>
<th>Age (years)</th>
<th>Catecholamine (pg/ml)</th>
<th>Noradrenaline (pg/ml)</th>
<th>Adrenaline (pg/ml)</th>
<th>Heart rate (beats/min)</th>
<th>Systolic blood pressure (Torr)</th>
<th>Diastolic blood pressure (Torr)</th>
<th>Pre-ejection period (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Untreated total population</strong></td>
<td></td>
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<tr>
<td>Normotensive (n = 28)</td>
<td>38.5 ± 1.7</td>
<td>315 ± 14</td>
<td>226 ± 20</td>
<td>89 ± 14</td>
<td>75 ± 1.5</td>
<td>117 ± 2.1</td>
<td>75 ± 1.6</td>
<td>88 ± 3.0</td>
</tr>
<tr>
<td>Labile hypertension (n = 21)</td>
<td>37.9 ± 2.0</td>
<td>528 ± 49**</td>
<td>286 ± 26*</td>
<td>242 ± 35**</td>
<td>90 ± 3.6**</td>
<td>140 ± 1.4**</td>
<td>88 ± 0.9**</td>
<td>80 ± 3.6</td>
</tr>
<tr>
<td>Sustained hypertension (n = 25)</td>
<td>43.4 ± 1.7*</td>
<td>461 ± 54*</td>
<td>370 ± 53**</td>
<td>91 ± 20</td>
<td>84 ± 2.4**</td>
<td>162 ± 3.3**</td>
<td>102 ± 1.8**</td>
<td>94 ± 3.1</td>
</tr>
</tbody>
</table>

**Untreated**

| Labile normoadrenergic (n = 9) | 36.8 ± 3.4  | 324 ± 44              | 208 ± 31             | 116 ± 39           | 79 ± 4.8                | 138 ± 6.1**                    | 88 ± 2.0**                    | 85 ± 3.1                 |
| Labile hyperadrenergic (n = 12) | 38.6 ± 2.5  | 683 ± 41**            | 345 ± 29**           | 338 ± 32**        | 96 ± 3.3**              | 141 ± 1.2**                    | 88 ± 0.9**                    | 79 ± 4.5                 |
| Sustained normoadrenergic (n = 16) | 42.9 ± 2.2  | 316 ± 33              | 235 ± 32             | 82 ± 21           | 80 ± 2.5               | 162 ± 10.7                     | 103 ± 2.5**                   | 99 ± 3.1                 |
| Sustained hyperadrenergic (n = 9) | 45.5 ± 2.8* | 716 ± 98**            | 612 ± 105**          | 104 ± 45          | 91 ± 4.4**              | 161 ± 5.5**                    | 102 ± 1.8**                   | 84 ± 5.7                 |

† Mean ± SEM.

* P < 0.05 vs normotensive.

** P < 0.01 vs normotensive.

**After propranolol**

|                  |               |               |               |               |                        |                                |                                |                          |
|------------------|---------------|---------------|---------------|---------------|------------------------|                                |                                |                          |
| Sustained normoadrenergic | 416 ± 50     | 322 ± 49     | 94 ± 24      | 65 ± 1.8      | 156 ± 5.1              | 99 ± 3.0                      | 105 ± 3.8                     |                          |
| Sustained hyperadrenergic | 479 ± 58     | 388 ± 40     | 91 ± 47      | 63 ± 5.3      | 137 ± 7.1*             | 92 ± 3.0*                     | 106 ± 13.1                    |                          |

* P < 0.05 vs sustained 'normoadrenergic' after propranolol.
cardiogram and electrocardiogram. Blood (9 ml) was sampled from a brachial vein for the determination of circulating CA. In patients with sustained hypertension, these procedures were repeated 2 weeks later after propranolol treatment at a dose of 160 mg/day.

Circulating CA were measured by a radioenzymatic method (Coyle & Henry, 1973) modified for measurements in serum (de Champlain et al., 1976). NA was measured on the same blood sample by another radioenzymatic assay (Henry, Starman, Johnson & Williams, 1975). Circulating adrenaline concentration levels were estimated by subtracting the NA value from the total CA value.

**Results**

Supine circulating CA and NA were significantly increased in labile and sustained hypertension (Table 1). The average total CA concentration was slightly higher in labile than in sustained hypertension but circulating NA concentrations were higher in sustained hypertension. In contrast, the estimated average adrenaline value was found to be markedly increased only in labile hypertensive patients. Mean heart rates were significantly increased in both groups of hypertensive patient. Pre-ejection period tended to be shorter in the labile hypertensive group and longer in the sustained hypertensive group.

When hypertensive patients were subdivided into ‘normoadrenergic’ (CA concentrations within normal range) and ‘hyperadrenergic’ (CA concentrations above normal range) subgroups, it was observed that ‘normoadrenergic’ labile and sustained hypertensive patients had a normal heart rate. However a longer pre-ejection period was observed in the latter subgroup. Although NA concentrations were significantly higher in both ‘hyperadrenergic’ labile and sustained hypertensive groups, these NA were considerably greater in the latter group of patients whereas adrenaline was increased exclusively in ‘hyperadrenergic’ labile hypertensive patients. Heart rates were elevated and pre-ejection period tended to be shorter in both groups of ‘hyperadrenergic’ patients.

After propranolol treatment, circulating CA and NA decreased in sustained ‘hyperadrenergic’ patients and no longer differed significantly from those in ‘normoadrenergic’ patients similarly treated (Table 1). Moreover, heart rate and pre-ejection period after propranolol were similar in both groups of hypertensive patients. However, the fall in systolic and diastolic blood pressure, the decrease in heart rate and lengthening in the pre-ejection period were significantly greater in the ‘hyperadrenergic’ group after propranolol.

**Discussion**

Supine circulating catecholamine concentrations were higher in labile and sustained hypertension but in sustained hypertension this increase was exclusively due to an increase in NA whereas in labile hypertension, it was mainly secondary to higher adrenaline concentrations. Elevated circulating CA could express a different type of sympathetic dysfunction. These observations are supported by the findings of increased adrenaline concentrations in labile and sustained hypertension (Franco-Morselli, Elghozi, Joly, Di Giulilio & Meyer, 1977). It is, however, premature to conclude whether these changes represent stages in the evolution of hypertension or whether they represent two distinct pathogenetic mechanisms.

Resting CA concentrations were higher than the normal range of values in about 50% of patients with labile hypertension and in about 30% of patients with sustained hypertension. ‘Hyperadrenergic’ labile or sustained hypertensive patients demonstrated signs of a hyperkinetic heart with higher heart rates and lower pre-ejection period values (Ibrahim, Tarazi, Dustan & Bravo, 1974). Moreover, ‘hyperadrenergic’ sustained hypertensive patients had higher CA response during standing (de Champlain et al., 1977). In contrast, ‘normoadrenergic’ hypertensive patients had normal cardiac functions and normal sympathetic response to postural stimulation. We previously suggested that these subgroups of ‘normoadrenergic’ and ‘hyperadrenergic’ hypertensive patients may represent different pathological entity (de Champlain et al., 1976).

After propranolol treatment, the decrease in systolic or diastolic blood pressure and in heart rate and the lengthening of pre-ejection period were greater in ‘hyperadrenergic’ than in ‘normoadrenergic’ hypertensive patients thus suggesting a greater contribution of the sympathetic system to the maintenance of hypertension and hyperkinetic cardiac functions in these patients. Propranolol decreased supine CA and NA concentrations in ‘hyperadrenergic’ hypertensive patients and restored to normal their increased sympathetic reactivity to postural changes, in agreement with the observation of others on the effects of prindolol and metoprolol on supine or standing CA concentra-
tions in hypertensive patients (Brecht, Banthier & Shoeppe, 1976; de Champlain et al., 1977).

The effects of β-adrenoreceptor blocking agents can be best explained by an action on presynaptic β-adrenoreceptors which would mediate a positive feedback mechanism on the liberation of NA by the sympathetic nerve (Yamaguchi, de Champlain & Nadeau, 1977). Propranolol could restore the increased sympathetic tone and reactivity of 'hyperadrenergic' patients by blocking the presynaptic positive feedback mechanism (de Champlain et al., 1977).

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References


