Baroreceptor Activity and Responsiveness to Angiotensin in Patients with Chronic Renal Failure

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It has been shown that in neurogenic (essential) hypertension baroreceptor sensitivity is decreased (Bristow et al, 1969). Apart from the observation of Gribbin et al (1970) that the baroreflex sensitivity did not change with dialysis and nephrectomy no systematic studies of baroreflex function have been performed in patients with chronic renal failure. Since the blood pressure regulation as well as the pathogenesis of hypertension in this condition are still poorly understood it seemed worth testing the baroreflex function in patients with chronic renal failure with and without hypertension in order to assess whether it is changed by renal failure as such. The application of angiotensin offered an opportunity to evaluate their pressor responsiveness as well – as for the susceptibility of subjects with insufficient renal function to exogeneous pressor substances, existing studies have given rather conflicting results (Augustin & Siemensen, 1972; Ducrot et al, 1969; Keynan et al, 1971).

METHODS AND SUBJECTS INVESTIGATED

Baroreceptor sensitivity was tested by the method of Smyth et al (1969). Angiotensin (Hypertensin Ciba) was injected in graded doses (0.25 - 1.5 ug) by means of a polyethylene cannula, 1 mm i d, into the femoral vein, blood pressure measured (capacitance manometer) by means of a red Kifa catheter in the femoral artery, respiratory cycle registered by means of a thermistor inserted in one nostril, and ECG (2nd standard lead) recorded in the usual way. All signals (including electric marking of injections) were amplified and registered using a Multiscriptor Hellige polygraph at a paper speed of 1 mm/sec (for assessing responsiveness to angiotensin) and 100 mm/sec (for testing the baroreflex function).

A total of 30 subjects was investigated; 16 were normotensive and 14 hypertensive (BP values 160/100 mm Hg and more). In the normotensive
group 4 subjects were in chronic renal failure (creatinine clearances 30 ml/min and less) while 12 had either satisfactory or normal renal function; in the hypertensive group the corresponding numbers were 9 and 5 respectively. No attempt was made to standardise their water and salt intake; however, their usual medication (except for immunosuppression in 7 allografted subjects) had been stopped at least 3 days before the investigation. Only two were dialysed.

The procedure was performed in fasting subjects during morning hours in a quiet room; there was an interval of at least 30 minutes between the insertion of catheters and the start of the investigation, and of 10 minutes between angiotensin injections. All personnel and registration devices were covered by a curtain so that the patients were not aware of the moment of the injection.

The responsiveness to angiotensin was assessed by the period of latency between the injection and BP increase, by the duration of BP elevation and by maximal increase in systolic and diastolic pressures. The baroreflex sensitivity in each individual was evaluated from the slope of the regression line between the systolic pressure and pulse interval (in msec increases in pulse interval for each 1 mm Hg rise in pressure) during expiration; only correlations significant at least at the 0.01 level were taken into consideration.

RESULTS

Table I. Means of slopes of different groups of subjects

<table>
<thead>
<tr>
<th>Group</th>
<th>number of subjects</th>
<th>specification</th>
<th>mean slope (msec/mm Hg)</th>
<th>statistical evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>chronic renal failure</td>
<td>13</td>
<td>regardless of BP values</td>
<td>4.220 ± 4.030</td>
<td>N.S.</td>
</tr>
<tr>
<td>satisfactory or normal</td>
<td>17</td>
<td></td>
<td>6.965 ± 4.185</td>
<td></td>
</tr>
<tr>
<td>renal function</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>chronic renal failure</td>
<td>9</td>
<td>paired by age and BP level</td>
<td>5.072 ± 4.615</td>
<td>N.S.</td>
</tr>
<tr>
<td>satisfactory or normal</td>
<td>9</td>
<td></td>
<td>7.063 ± 7.084</td>
<td></td>
</tr>
<tr>
<td>renal function</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>normotensives</td>
<td>16</td>
<td>regardless of renal function</td>
<td>7.081 ± 4.202</td>
<td>N.S. (0.05 &lt; p &lt; 0.10)</td>
</tr>
<tr>
<td>hypertensives</td>
<td>14</td>
<td></td>
<td>4.282 ± 4.088</td>
<td></td>
</tr>
<tr>
<td>normotensives</td>
<td>8</td>
<td>regardless of renal function paired by sex and age</td>
<td>6.247 ± 2.235</td>
<td>N.S. (0.05 &lt; p &lt; 0.10)</td>
</tr>
<tr>
<td>hypertensives</td>
<td>8</td>
<td></td>
<td>4.077 ± 2.531</td>
<td></td>
</tr>
</tbody>
</table>

Table I shows that no significant differences were present in the mean slopes of regression lines between subjects with creatinine clearances below and above 30 ml/min, both when all subjects were included regardless of BP values and when selected and paired by age and BP levels. Similarly the differences between normotensives and hypertensives did not reach statistical significance. As demonstrated by Figure 1 there was a correlation between the slopes and age, and between the slopes and resting values of
systolic blood pressure. No differences were found in responsiveness to angiotensin between renal failure patients and subjects with satisfactory or normal renal function (Table II).

DISCUSSION

Baroreflex sensitivity in our patients with chronic renal failure did not differ markedly from that in subjects with satisfactory or normal renal function; however, the evaluation of baroreceptor function in the former offers some difficulties. It may be suspected that with a variety of factors influencing both cardiac activity (tachycardia associated with anaemia, latent heart failure, etc) and pressor response to angiotensin (eg different states of sodium and water balance – Andersson et al, 1972; Brunner et al, 1972) the interrelationship between blood pressure increase and cardiac slowing is modified: disturbed baroreceptor control in chronic uraemia was described by Cohn et al (1966). This may be the explanation of both the considerable scatter of individual slopes and their slightly lower mean value in subjects with renal failure in the present series. For a definite assessment of baroreflex function in this condition a substantially larger group of investigated subjects may be necessary, allowing either a multiple regression analysis (Gribbin et al, 1971) or pairing by sex, age and blood pressure in order to differentiate all factors influencing it; however, as the most probable explanation of a decrease in sensitivity is loss of arterial distensibility (Sleight, 1971), as suggested also by a difference between stage 1 and 2 (World Health Organisation, 1962) hypertensives (Jirka & David, 1973, unpublished), a change produced by uraemia itself is hardly to be expected.

Likewise we did not observe a significant difference in baroreflex sensitivity between our normotensives and hypertensives. Since the reason is hardly a qualitative one, the most probable explanation is either the already discussed scatter of individual values or different criteria for diagnosis of hypertension than those used by Bristow et al (1969) or both. We classified our subjects as normotensives or hypertensives not according to their resting pressures during the investigation, but on the basis of their casual pressures before the investigation (most of them had been seen periodically in the out-patient department), which we think is more correct, the more so because in subjects with previous hypertension baroreceptor sensitivity may be decreased even though their actual blood pressure is normal (Gribbin et al, 1971). Both explanations seem to be valid: the correlation between resting systolic pressure and age and baroreflex sensitivity in our subjects is similar to that found by Bristow et al (1969) and Gribbin et al (1971) in persons free of renal disease and with essential hypertension, and shows that in this respect renal hypertension resembles essential hypertension.
Our data concerning responsiveness of renal failure patients to angiotensin are in agreement with results obtained by other techniques (Ducrot et al, 1969; Keynan et al, 1971).

SUMMARY

1. Baroreflex function and responsiveness to injections of angiotensin (0.25 and 0.50 µg) were assessed in subjects with renal failure (4 normotensives and 9 hypertensives) and normal renal function (12 normotensives and 5 hypertensives). Creatinine clearances were below 30 ml/min in the first group.

2. No modification of these parameters was found which might be explained by renal failure alone. Baroreflex sensitivity in hypertension due to chronic renal failure showed a similar correlation with age and blood pressure as in essential hypertension.

ACKNOWLEDGMENTS

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