Dopa, catecholamines and their metabolites in essential hypertension

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Summary

1 Urinary excretion of dopa, catecholamines and their metabolites (vanillylmandelic acid, methoxy-catecholamines, 3-methoxy-4-hydroxyphenylglycol and homovanillic acid) were studied in eighty patients with essential hypertension and in twenty-five healthy control subjects.

2. Increased urinary excretion of catecholamines, dopa and catecholamine metabolites was found in a proportion of cases.

3. The relationship between urinary excretion of catecholamine metabolites and the excretion of dopa and noradrenaline was found in a proportion of cases.

4. In view of the suggested significance of 3-methoxy-4-hydroxyphenylglycol as an index of brain catecholamine metabolism, particular attention was paid to urinary excretion of this metabolite in the subjects under study.

Key words: catecholamines, dopa, essential hypertension, 3-methoxy-4-hydroxyphenylglycol.

Introduction

Numerous studies indicate increased sympathetic activity in a proportion of patients with essential hypertension, as reflected by augmented blood catecholamine concentrations and enhanced urinary excretion of catecholamines and their metabolites (Engelman, Portnoy & Sjoerdsma, 1970; De Quattro, 1971; Esler & Nestel, 1973; Louis, Doyle & Anavekar, 1973).

An earlier study by our group has shown that the population of patients with essential hypertension is not homogeneous in the pattern of urinary excretion of noradrenaline (Januszewicz & Wocial, 1975). Noradrenaline excretion has been found to be increased in about 9% of our patients, decreased in about 6%, and normal in the remaining cases.

In the present study we have attempted to gain a deeper insight into the metabolism of catecholamines in these three sub-groups of patients by assessing urinary excretion of dopa, dopamine, and catecholamine metabolites, namely methoxycatecholamines, vanillylmandelic acid, 3-methoxy-4-hydroxyphenylglycol and homovanillic acid.

Methods

Patients

Eighty in-patients with essential hypertension were studied. Throughout the study the patients did not receive hypotensive drugs or other medication which might have influenced catecholamine metabolism or interfered with the results of chemical methods. They received a standard hospital diet. Known causes of secondary hypertension were excluded by careful diagnostic procedures. All patients were free from congestive heart failure and renal failure.

Urinary excretion of noradrenaline was normal in forty-five patients; it was increased in twenty (five female, fifteen male) and decreased in fifteen (five female, ten male). The mean ages of the patients in these three groups were 36, 38 and 33 years respectively.

The control group consisted of twenty-five healthy subjects (eleven female, fourteen male) aged 21–54 years (mean age 33.8 years).

Determinations

The following methods were used for determin-
<table>
<thead>
<tr>
<th></th>
<th>No. of patients</th>
<th>Age (years)</th>
<th>Noradrenaline (μg/24 h)</th>
<th>Adrenaline (μg/24 h)</th>
<th>Dopamine (μg/24 h)</th>
<th>Dopa (μg/24 h)</th>
<th>VMA (mg/24 h)</th>
<th>MNA + MA (μg/24 h)</th>
<th>MHPG (μg/24 h)</th>
<th>HVA (mg/24 h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential hypertension</td>
<td></td>
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<tr>
<td>Noradrenaline normal</td>
<td>45</td>
<td>36±2 (16–65)</td>
<td>19.8±4.4</td>
<td>3.2±1.4</td>
<td>254.9±40.9</td>
<td>52.0±8.7</td>
<td>5.7±1.4</td>
<td>534.3±174.6</td>
<td>699.6±70.9</td>
<td>7.1±0.7</td>
</tr>
<tr>
<td>Noradrenaline high</td>
<td>20</td>
<td>37±6 (17–62)</td>
<td>38.5±4.4</td>
<td>4.1±2.0</td>
<td>247.5±39.3</td>
<td>46.3±11.9</td>
<td>4.8±1.2</td>
<td>680.1±210.7</td>
<td>868.3±143.9</td>
<td>6.6±1.0</td>
</tr>
<tr>
<td>Noradrenaline low</td>
<td>15</td>
<td>32±7 (16–55)</td>
<td>8.5±1.1</td>
<td>2.3±1.2</td>
<td>299.5±22.9</td>
<td>66.8±12.9</td>
<td>7.1±1.3</td>
<td>454.0±100.2</td>
<td>628.5±90.4</td>
<td>7.2±0.6</td>
</tr>
<tr>
<td>Control subjects</td>
<td>25</td>
<td>33±8 (21–56)</td>
<td>22.2±6.1</td>
<td>4.1±1.6</td>
<td>293.0±36.0</td>
<td>46.1±10.1</td>
<td>4.1±1.2</td>
<td>647.0±207.1</td>
<td>650.1±120.0</td>
<td>7.2±2.1</td>
</tr>
</tbody>
</table>

Table 1. Urinary excretion of noradrenaline, adrenaline, dopamine, dopa and their metabolites [vanillylmandelic acid (VMA), methoxycatecholamines (MNA+MA), 3-methoxy-4-hydroxy phenylglycol (MHPG) and homovanillic acid (HVA)] in patients with essential hypertension

Mean values ± sd are shown.
ation of catecholamines and metabolites in the urine.

Noradrenaline and adrenaline. Trihydroxyindole fluorimetric method of Euler & Lishajko (1961): recovery 88 ± 12%, and 89 ± 9% respectively.

Dopamine. Fluorimetric method of Carlsson & Waldeck (1958): recovery 89 ± 4.4%.


Vanillylmandelic acid (VMA). Colorimetric method of Pisano, Crout & Abraham (1962): recovery 84.2 ± 3.4%.

Dopamine. Fluorimetric method of Anton & Sayre (1964): recovery 83 ± 9%.

Homovanillic acid (HVA). Colorimetric method, after separation by thin-layer chromatography according to Sankoff & Sourkes (1963): recovery 82 ± 6.9%.

3-Methoxy-4-hydroxyphenylglycol (MHPG). Fluorimetric method of Antun, Pullar & Eccleston (1971): recovery 79.2 ± 11%.

Student's t-test was used for statistical analysis.

Results
The results are summarized in Table 1. Urinary excretion of adrenaline was significantly lower in low-noradrenaline excretors than in high-noradrenaline excretors (P < 0.01) and in the control group (P < 0.01). Excretion of dopamine in patients excreting normal amounts of noradrenaline and in high-noradrenaline excretors was significantly lower than in control subjects (P < 0.01), and in low-noradrenaline excretors (P < 0.01). It is noteworthy that excretion of dopamine by low-noradrenaline excretors did not differ significantly from the control value (P > 0.1). Low-noradrenaline excretors were found to excrete larger amounts of dopa than the other groups of patients, and excretion of dopa by high-noradrenaline excretors was significantly lower than that of the remaining two groups of patients (P < 0.01 in both instances) and the control subjects.

The highest excretion of MNA + MA (1) was found in patients with increased noradrenaline excretion; there was no significant difference in MNA + MA excretion of the groups with normal and low excretion of noradrenaline (P > 0.1).

(1) Abbreviations: MNA + MA, methoxycatecholamines; HVA, homovanillic acid; MHPG, 3-methoxy-4-hydroxyphenylglycol; VMA, vanillylmandelic acid.

Urinary excretion of VMA was higher in low noradrenaline excretors than in the other groups of patients (P < 0.01 in both instances).

MHPG excretion was the highest in high noradrenaline excretors and exceeded significantly the values found in the other two groups of patients (P < 0.01 in both cases). Urinary excretion of HVA was similar in the three groups (P > 0.1).

Discussion
The results of this study disclose differences in urinary excretion of dopa, dopamine and catecholamine metabolites in patients with essential hypertension, depending on the pattern of excretion of noradrenaline. It is noteworthy that high-noradrenaline excretors demonstrate decreased excretion of dopa and dopamine. This decrease is probably not due to enhanced metabolism, as indicated by normal excretion of HVA.

Interestingly, increased excretion of noradrenaline is paralleled by augmented excretion of MHPG. This finding may indirectly indicate enhanced metabolism of noradrenaline in the central nervous system, since it has been shown experimentally that about 30% of urinary MHPG is derived from metabolism of noradrenaline in the brain (Maas & Landis, 1968). A question emerges as to the possible role of altered brain noradrenaline metabolism in the pathogenesis of hypertension in this sub-group of patients. The lack of unidirectional changes in the excretion of VMA and MHPG in high-noradrenaline excretors may indicate altered activity of enzymes involved in the formation of these metabolites.

It should be pointed out that low-noradrenaline excretors exhibit increased excretion of dopa and a different pattern of metabolite excretion.

Our data demonstrate distinct differences in the pattern of various noradrenaline precursors and metabolites excreted in the urine of patients with essential hypertension, depending on increase or diminution of sympathetic activity. This may be considered yet another indication of differences in catecholamine metabolism within the population of patients with essential hypertension.

The mechanisms regulating catecholamine synthesis, release and metabolism are very complex but their further study may well contribute to a better understanding of the role of sympathetic activity in the pathogenesis of essential hypertension.
References


