recent data support this hypothesis. Stemming from their observation that high dietary sodium intake decreases norepinephrine release in the anterior hypothalamus of SHR. Oparil and colleagues hypothesized that high dietary sodium intake increases $\alpha_2$-adrenergic receptor density (receptor up-regulation secondary to decreased norepinephrine release) in the anterior hypothalamus of SHR. These investigators found that high dietary sodium intake in SHR increased $\alpha_2$-adrenergic receptor density in the anterior hypothalamus but had no effect on $\alpha_2$-adrenergic receptor affinity.

Thus, the in vivo functional data of our study and the in vitro radioligand binding data of Oparil and colleagues are complementary. Together, these studies point to the conclusion that high dietary sodium intake increases the responsiveness or sensitivity (defined functionally in vivo and biochemically in vitro) of central nervous system $\alpha_2$-adrenergic receptor control of renal sympathetic nerve activity and urinary sodium excretion.

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References


Individualization of Antihypertensive Therapy

To the Editor:

To our mutual surprise, we discovered in the February 1988 issue of Hypertension the simultaneous publication of two independent investigations performed in our respective groups. The coincidence encouraged us to follow up on the approach we were using independently—to improve the care of our hypertensive patients by individualizing their therapy through a more precise analysis of the fall in blood pressure induced in each patient by the sequential administration of two or more antihypertensive drugs. At present, the selection of a drug for an individual hypertensive patient is usually based on trends derived from large-scale randomized clinical trials, on various rigid stepped-care programs recommended for current practice, or on indices such as age, renin, or race, whose predictive value for the antihypertensive efficacy of a given...
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drug has been suggested by statistically significant correlations valid for large groups of selected and heterogeneous patients. Improvements in the evaluation of blood pressure changes used together with appropriate designs for sequential drug administration will allow for a more precise analysis of the efficacy of drugs in a given patient, thus offering a clinically based approach for optimization of individual therapy.

Group analysis of the antihypertensive effect of two antihypertensive treatments conceals behind its global result a variable proportion of individual good responders, nonresponders, and possibly even some patients who experienced a pressure increase. Even if the average effect of Drug A is less pronounced than that of Drug B, Drug B may still be more efficacious in some individuals than Drug A. The use of an individualized choice of therapy based on sequential trial and error ultimately provides, for a group of patients, a bigger decrease in blood pressure than can be achieved by the systematic prescription of the drug considered to be most effective in a classic group analysis. It also detects among the group of treated patients those individuals who are insensitive to all tested treatments. This is demonstrated in Table 1, which is based on the three recent reports by our research groups on the results of crossover evaluation of antihypertensive drugs. Clearly, in each of the studies, choosing the best response to either of the drugs markedly enhances the blood pressure reduction that can be obtained by single-drug antihypertensive therapy (see the last column in Table 1).

The multiplication of blood pressure measurements through self-recording at home or 12- to 24-hour continuous monitoring greatly improves the accuracy of the blood pressure result, and these methods also eliminate the physician-induced blood pressure rise known as the white coat effect. If such end-point monitoring is used jointly with the technique of crossover design, the trial and error evaluation of antihypertensive drugs may become more scientifically useful, but carry-over effects must be eliminated, and future studies should establish that the antihypertensive effect of a given drug is reproducible in an individual patient. Obviously, the treating physician should always know the dose-response curve for the individual drug's efficacy, the time needed until a steady state effect is reached, and the duration of its action with repeated administration. For a patient who will have to take medicine every day for many years, however, it is certainly not a waste of time if the carefully planned and analyzed initiation of therapy lasts for a few months. Such optimization of antihypertensive therapy should benefit the individual patient, and very likely it would also enhance the difference in the incidence of cardiovascular events between "permanently treated" and truly well controlled hypertensive patients.

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References

Table 1. Comparison of Systematic and Individualized Antihypertensive Treatment

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Average fall in diastolic BP (mm Hg)</th>
<th>No. of non-responders to both treatments</th>
<th>Average fall in diastolic BP (mm Hg) in responders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bidiville et al.</td>
<td>Enalapril</td>
<td>13.8±2 (n=16)</td>
<td>2/16</td>
<td>15.3±1.9 (n=8)</td>
</tr>
<tr>
<td></td>
<td>Diltiazem</td>
<td>10.3±2 (n=16)</td>
<td></td>
<td>11.6±2.1 (n=6)</td>
</tr>
<tr>
<td>Ménard et al.</td>
<td>Oxprenolol</td>
<td>3.7±6.0 (n=24)</td>
<td>9/24</td>
<td>4.9±7.1 (n=6)</td>
</tr>
<tr>
<td></td>
<td>Chlorthalidone + Triamterene</td>
<td>4.0±6.7 (n=24)</td>
<td></td>
<td>7.3±6.3 (n=9)</td>
</tr>
<tr>
<td>Waebner et al.</td>
<td>Betaxolol</td>
<td>7.8±1.9 (n=17)</td>
<td>3/17</td>
<td>9.9±1.8 (n=9)</td>
</tr>
<tr>
<td></td>
<td>Verapamil</td>
<td>3.0±1.9 (n=17)</td>
<td></td>
<td>3.8±2.2 (n=5)</td>
</tr>
</tbody>
</table>

Values are means ± SEM. BP = blood pressure; responders are those with a diastolic BP decrease of 5 mm Hg or more.
*Average fall in diastolic BP for each trial drug after excluding the nonresponders.
†Average fall in diastolic BP taking into account only the best response to either drug. In this column, n = number of patients with best response to the drug specified.


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