Dopaminergic Control of Prolactin and Blood Pressure

To the Editor:

We read with great interest the paper of Sowers et al. about the dopaminergic control of prolactin (PRL) in essential hypertension (Sowers JR, Nyby M, Jasberg K: Dopaminergic control of prolactin and blood pressure; altered control in essential hypertension. Hypertension 4 (431-438, 1982). We also have found evidence favoring the existence of a deranged dopaminergic system in low-renin essential hypertension (LREH).

We report herein our findings in a group of five patients diagnosed as having LREH (defined by being below 45 years of age, having normal renal function, serum potassium above 3.5 mEq/liter, plasma renin activity (PRA) below 3 ng/ml/hr, after 3 hours of rest while on a 10 mEq sodium diet, and normal urinary excretion of aldosterone while on 10 mEq and 110 mEq sodium diets). We explored the function of the hypothalamic-pituitary axis by studying: 1) the response of thyrotropin (TSH) and PRL to TRH administration (200 /Lig i.v.); 2) the response of cortisol and growth hormone (GH) to insulin-induced hypoglycemia; 3) the response of FSH and LH to LHRH administration; 4) the urinary excretion of free cortisol. The values obtained were compared with those obtained in a control group of five normotensive volunteers (CG) and those of a group of 15 patients diagnosed as having normoreninemic essential hypertension (NEH). The response of cortisol and GH to insulin-induced hypoglycemia and that of FSH and LH to LHRH was similar in the three groups studied. Nevertheless, the response of TSH and PRL to TRH was abnormally high, as can be seen in table 1. It is well established that the regulation of both hormones is mediated by the dopaminergic system, and our results point to the existence of a deranged dopaminergic system in LREH.

Table 1. Response of Prolactin and Thyrotropin to TRH Administration in Normotensive Controls (CG), Patients with Low-Renin Hypertension (LREH), and Patients with Normoreninemic Essential Hypertension (NEH)

<table>
<thead>
<tr>
<th>Subjects</th>
<th>-15 min</th>
<th>0</th>
<th>15 min</th>
<th>30 min</th>
<th>60 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolactin response (ng/ml)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CG</td>
<td>10.2±0.9</td>
<td>9.1±0.8</td>
<td>49.1±8.3</td>
<td>34.2±6.4</td>
<td>22.6±7.1</td>
</tr>
<tr>
<td>NEH</td>
<td>14.9±1.4</td>
<td>12.3±1.0</td>
<td>55.2±9.6</td>
<td>36.4±5.8</td>
<td>24.6±6.1</td>
</tr>
<tr>
<td>LREH</td>
<td>11.6±2.1</td>
<td>10.9±1.8</td>
<td>95.6±11.6*</td>
<td>88.5±9.3*</td>
<td>47.5±5.8*</td>
</tr>
<tr>
<td>Thyrotropin response (mU/ml)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CG</td>
<td>2.5±1.4</td>
<td>3.2±2.0</td>
<td>14.4±7.3</td>
<td>17.8±6.9</td>
<td>9.6±3.8</td>
</tr>
<tr>
<td>NEH</td>
<td>2.9±1.8</td>
<td>3.0±1.8</td>
<td>16.2±8.0</td>
<td>17.0±5.8</td>
<td>12.1±4.7</td>
</tr>
<tr>
<td>LREH</td>
<td>3.8±2.1</td>
<td>3.5±2.1</td>
<td>23.6±7.1*</td>
<td>27.4±8.5*</td>
<td>20.2±5.7*</td>
</tr>
</tbody>
</table>

*p < 0.01 (vs GC and NEH)

Values are expressed as means ± SEM.

References


Authors’ Response:

The observation by Robles et al. that a small group of patients with low-renin essential hypertension (LREH) have exaggerated thyrotropin (TSH) and prolactin (PRL) responses to TRH is very interesting. Studies conducted in our laboratory several years ago1,2 demonstrated that spontaneously hypertensive rats (SHR) have exaggerated TSH and PRL responses to TRH as well as stress. In our hands the SHR has been a low renin model of hypertension. Thus, the exaggerated TSH and PRL responses to TRH in LREH in humans are analogous to the observations in the low renin SHR model of essential hypertension. As noted by Robles et al., it appears that dopaminergic mechanisms regulate the secretion of both TSH and PRL in mammals. We previously proposed that exaggerated PRL responses to TRH and stress reflect alterations in central dopaminergic control of PRL secretion. That alterations in central and peripheral control of PRL and corticosteroid secretion may play a role in the pathogenesis of high blood pressure in the SHR and in humans with essential hypertension is suggested by sev-
eral observations. Treatment with the dopamine agonist bromocriptine causes parallel decreases in plasma PRL, sympathetic tone, and blood pressure in SHR and in patients with essential hypertension without lowering resting supine blood pressure in normotensive rats and humans.10

Although it is likely that exaggerated PRL responses to TRH and stress in the SHR and hypertensive humans probably reflect altered dopaminergic regulation of PRL secretion and blood pressure, it is possible that PRL may have a direct role in the pathogenesis of hypertension in the SHR and in LREH. PRL administration has been reported to increase blood pressure in rabbits4 and rats.9 Recently, it was reported that postnatal administration of antisera to rat PRL resulted in a significant lowering of pressure in SHR at 14 weeks of age.10 These results were interpreted as suggesting that endogenous PRL is involved in blood pressure regulation.10 We have recently observed elevated blood pressures in 20 rats transplanted with PRL-secreting mammotrophic tumors (MitTF4) compared to sham transplanted controls (table 1). Further, there was a positive correlation (r = 0.67) between PRL levels and blood pressures in these tumor-transplanted rats. These observations suggest a possible direct role for elevated endogenous PRL levels in the pathogenesis of high blood pressure in the SHR and in a subset of patients with essential hypertension. Since PRL levels rise in response to a variety of conditions including mental and physical stress, perhaps posture and isometric exercise and sleep, it is possible that exaggerated PRL responses to these stimuli and secondarily elevated endogenous PRL levels could play a role in the pathogenesis and/or maintenance of hypertension.

References

JAMES R. SOWERS, M.D.
Associate Professor of Medicine
UCLA School of Medicine
Sepulveda VA Medical Center
Sepulveda, California 91343

The Age Factor and Salt-Induced Hypertension in the Brattleboro Rat
To The Editor:

As a coauthor of papers on salt-induced hypertension in Brattleboro rats,1° I should like to comment on the discussion of Gruber vs Berecek and Crofton (Hypertension 4: 572–574, 1982). A moderate salt hypertension was elicited in uninephrectomized DI rats exposed from prepuberty to high salt intake, while no hypertension occurred in DI rats that were influenced by very high salt intake only in adulthood (250 mmoles/kg/day for 14 weeks). This is not in apparent conflict with the findings of Crofton et al.5 and Berecek et al.4 The lower salt sensitivity of DI animals was confirmed when hypophysosupravalve was infused into adult nephrectomized DI rats. Only 50% of the blood pressure increase observed in Wistar rats was elicited in DI rats.7 The existence of a vasopressin-independent component of increased blood pressure argues against the resistance of vasopressin-deficient animals to the hypertensogenic action of salt. Thus, the failure to induce DOC-salt hypertension in DI rats5 need not be caused only by the use of adult animals. Relatively low salt intake (as compared to our experiments) and/or a difference in the stimulus provided by the DOC-salt regimen could be important factors, as well. Our data indicated that vasopressin was not essential for the pathogenesis and/or maintenance of salt hypertension, but the data did not rule out an important modulatory role for vasopressin in this kind of hypertension. However, if dDAVP can substitute for vasopressin, a the direct pressor role of vasopressin seems to be of minor importance in DOC-salt hypertension.

Our most important finding was that the susceptibility of DI rats to the hypertensive effects of uninephrec-
Dopaminergic control of prolactin and blood pressure.
R Garcia-Robles, L Ruilope, A Hurtado, J Rodicio and J Sancho

Hypertension. 1983;5:155-156
doi: 10.1161/01.HYP.5.1.155

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1983 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/5/1/155.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/