Anxiety, Anger, and Neurogenic Tone At Rest and in Stress in Patients with Primary Hypertension

PATRICK SULLIVAN, M.D., SARAH SCHOENTGEN, M.S., VINCENT DEQUATTRO, M.D., WARREN PROCII, M.D., DANIEL LEVINE, M.D., JOSEPH VAN DER MEULEN, M.D., AND JOSEPH BORNHEIMER, M.D.

SUMMARY To determine whether basal blood pressure or pressor responses to stress are related to sympathetic nerve tone or to psychological factors in hypertensives, 15 hypertensives and 13 normotensives were studied by means of a self-administered questionnaire, isometric handgrip exercise (IHE), and the mental stress of serial subtraction. Plasma norepinephrine (NE), epinephrine (E), blood pressure (BP) and heart rate (HR) were measured before and at the end of IHE and mental stress. A greater number of hypertensives had suppressed anger ($p < 0.01$) and scored higher on anxiety trait ($p < 0.01$) and depression ($p < 0.05$). Prestress (IHE and mental) BP and NE values were significantly greater in hypertensives (all $p < 0.01$). During IHE, both groups had a significant increase of BP, HR, and NE (all $p < 0.01$) but E rose in hypertensives only ($p < 0.05$). The percentage change of BP, HR, NE, and E during IHE was similar in both groups. The changes of BP and HR were not related to NE or E. During mental stress, HR ($p < 0.01$) and E ($p < 0.05$) increased in both groups. However, BP (systolic and diastolic) increased in normotensives only ($p < 0.01$). Plasma NE contents were unchanged in both groups. There were significant positive correlations of anxiety trait with systolic BP ($p < 0.05$), diastolic BP ($p < 0.05$), and NE ($p < 0.05$) and E ($p < 0.05$). Although hypertensives had increased neurogenic tone related perhaps to inward anger and anxiety, the percentage responses of neurogenic tone and BP to IHE were equivalent to those of normotensives. The challenge of serial subtraction did not elicit further noradrenergic or pressor responses in hypertensives. Suppressed anger and anxiety, via increased basal neurogenic tone, may be pathogenic factors in some patients with primary hypertension. (Hypertension 3 (suppl II): II-119–II-123, 1981)

KEY WORDS • plasma norepinephrine • epinephrine • psychological profile • isometric exercise

ENHANCED sympathetic nerve tone may be a causal factor in primary hypertension. A recent review of the studies of resting plasma norepinephrine (NE) in primary hypertension supports the earlier findings of raised NE in some of these patients. Young males with borderline hypertension and high plasma renin activity (PRA) had an association of raised NE and increased prevalence of suppressed anger. The present study was meant to relate resting blood pressure and neurogenic tone of uncomplicated hypertensives to their responses during physical and mental stress in the framework of their psychological profile of anger, anxiety and depression. Suppressed anger and anxiety, via increased basal neurogenic tone, appear to be pathogenic in some of our patients with primary hypertension.

Methods

Patients

We studied 15 patients with primary hypertension, aged 37 ± 11 years (mean ± SEM), whose average blood pressure (BP) exceeded 140/90 mm Hg on three separate occasions and 13 normotensive volunteers (36 ± 8 years). None of the patients had cardiovascular or renal sequelae of their hypertension or received antihypertensive medication within 3 weeks of the studies. Sixty percent of the hypertensives were females as compared with 30% of the normotensives; 60% of the hypertensives and 55% of the normotensives were Caucasian.
Protocol

All patients signed an informed consent approved by the Institutional Review Committee after being apprised of the nature of the study and the attendant potential risks. They were admitted to the Clinical Research Center of the Los Angeles County-USC Medical Center and begun on a constant diet containing 100 mEq Na⁺ and 80 mEq K⁺. Both patients and volunteers (studied in a similar manner but as outpatients) fasted overnight and did not smoke or take tea or coffee during the assessment period. Daily 24-hour urines were collected for sodium. Personality profiles were obtained on the day of admission through a self-administered written psychometric instrument testing depression and anxiety levels, tendency to repress anger, guilt about the expression of anger, and various aspects of direct and indirect hostility. The instrument was a multiple-choice questionnaire composed of four standard scales: the Beck Depression Inventory, the Spielberger State-Trait Anxiety Inventory, a modified and expanded version of an Anger-In/Anger-Out scale used by Harburg et al., and the Buss-Durkee Hostility Inventory.

Blood pressure, pulse rates, and venous blood from an indwelling needle were obtained in the morning of Day 2 after sitting 30 minutes and again at the end of 3 minutes of isometric handgrip exercise (IHE). The IHE consisted of a workload of 30% of maximum voluntary contractions. On Day 4 the experiment was repeated but the stress was 10 minutes of serial subtraction of numbers enforced by a metronome. Measurements and blood were taken during the last 2 minutes of the serial subtraction.

Assays

Plasma was separated from heparinized blood on ice and stored at −20°C. Norepinephrine and epinephrine (E) were measured by the radioenzymatic assay method of Peuler and Johnson. Urinary Na⁺ was measured by flame photometry. Coefficients of variation for NE and E were 7.4 and 8.5% respectively.

Statistics

The questionnaires were scored by computer and responses of hypertensives were compared to those of normotensives by Student t tests and chi-square analysis. The change in each parameter from pre- to post-stress was analyzed within groups by paired t tests. The mean percent change from pre- to post-stress was compared between the groups by two-sample t tests. Correlation analyses were performed to test relationships among the changes in the hemodynamic and biochemical parameters, as well as their associations with personality measures.

Results

Blood Pressure and Pulse Rate Responses to Isometric Handgrip Exercise (IHE) and Mental Stress

The arterial BP of hypertensives was 153 ± 15/104 ± 9 and 144 ± 15/96 ± 13 mm Hg prior to IHE and mental stress, respectively. Values for normotensives were 109 ± 12/73 ± 11 and 104 ± 12/70 ± 10 mm Hg (fig. 1). The isometric stress produced significant increments of systolic and diastolic blood pressures of 5% to 10% and pulse rates of 8% to 15%, and were of similar magnitude for both groups (fig. 2). Mental stress produced similar responses in the normotensives. However, heart rate and E increased after mental stress in hypertensives without changes in BP (fig. 3). The difference in systolic BP responses between the two groups, after mental stress, was significant (p < 0.01) (fig. 3).

Resting Plasma Catecholamines and Responses to Stress

The plasma concentration of NE of the hypertensives was 438 ± 45 ng/liter and 468 ± 43 ng/liter, sitting, before exercise and mental stress, respectively. Values for normotensives were 306 ± 27 and 353 ± 23 ng/liter, p < 0.05 (fig. 1). Pre-stress E levels were 58 ± 16 and 51 ± 10 ng/liter respectively, in hypertensives and were not significantly different from normotensives (44 ± 5 and 44 ± 8). NE increased approximately 33% in response to IHE in both groups. There was a greater increase in E in hypertensives (80%)
SYMPATHOADRENAL HYPERACTIVITY IN HYPERTENSION/Sullivan et al.

Figure 2. Effects of isometric stress on blood pressures, pulse rates, and catecholamines. The increment in pressures, pulse rates, and catecholamines was similar for both groups.

Figure 3. Effects of mental stress on blood pressures, pulse rates, and catecholamines. There were no significant changes of blood pressure or NE in hypertensives after mental stress. Pulse rates and E were increased in both groups.

compared with normotensives (40%), but the difference was not significant (fig. 2). There was a 50% increment in E, but no significant change in NE in the response to mental stress in both groups (fig. 3). There was an inverse correlation between the change in NE during mental stress and the basal NE in both the hypertensives ($r = -0.37$) and the normotensives ($r = -0.35$). However, neither was significant.

Psychological Profile

Fifty-three percent of primary hypertensives displayed "anger-in," a threefold greater prevalence rate than that of normotensives (18%), $p < 0.01$. Hypertensives also had increased scores for anxiety trait ($p < 0.05$) and depression ($p < 0.05$), but their hostility scores resembled those of normotensives (fig. 4).

Correlation analyses of the psychological features of all subjects with their basal measurements revealed a significant linking of anxiety trait with systolic ($r = 0.41$, $p < 0.05$), and diastolic BP ($r = 0.37$, $p < 0.05$) and with NE ($r = 0.38$, $p < 0.05$). On the other hand, we found no significant relationship between the changes of BP and HR during both IHE and mental stress with the changes in plasma catecholamines. The direct relationships of anxiety state and depression with the changes in heart rate after IHE were not significant ($r = 0.41, 0.40$, respectively). Further, the inverse relationship of "anger-in" and systolic BP response to IHE ($r = -0.25$) was not significant. Neither did the inverse relationship of anxiety trait with the change of NE after mental stress ($r = -0.28$) reach significance.

Discussion

Plasma NE at rest was increased in hypertensives. Two types of group differences could have obscured the findings. First, there were more females in our hypertensive sample. However, analyses of NE contents separately by gender confirmed the increased hypertensive values. Further, hypertensives were evaluated as inpatients and normotensives as outpatients. Previously we found that plasma NE in hypertensives exceeded that of normotensives whether the groups were studied in or out of the hospital. A recent report confirmed that hypertensives have identical plasma NE values whether in or out of the hospital.

The pressor responses of our subjects to IHE were similar to those of untreated hypertensives and normotensives reported previously. The changes we observed in NE in both our groups after IHE were similar to those of others at 3 minutes. The E responses of our subjects were of an intermediate magnitude compared to those of others. In previous comparative studies of NE after IHE, values were lower in hypertensives at 4 to 5 minutes and of equal magnitude at 3 minutes. Our "contrived" mental stress seemed inadequate, inasmuch as the pressor response in normotensives was approximately one-half that described previously. However, our findings
confirmed the E pattern of response to psychological stress. There was weak evidence that noradrenergic responses to "contrived" stress were least in patients with higher basal NE, perhaps by distracting them from their "global" anxiety. We agree that studies using "noncontrived" mental stress, where E increased three- to fourfold, would be preferable.

Investigators as far back as 1918 have described a cluster of values and attitudes among their hypertensive patients. Moschowitz reported a "restrained" type of personality. In 1939, Alexander reviewed the evidence for a vicious cycle produced by excessive inhibitions in the etiology of essential hypertension. In the 1950s, Saslow et al. reported subnormal assertiveness in hypertension, and Dunbar described hypertensives as afraid to show anger with an excessive desire to please. In 1961, Buss discussed the importance of suppressed rage in the etiology of hypertension. In 1970, Reiser distinguished between psychological conditions that may lead to the activation of hypertension and psychological states that may be activated by the disease and then later affect its course. Harburg et al. in a study of young college males, found that anxiety and neuroticism levels correlated strongly with BP lability. The 1973 study of Harburg et al. of suppressed hostility and guilt feelings about the expression of anger reported significant relationships between withheld anger and BP levels. In 1977, Esler et al. performed psychometric testing of high and normal renin, young, male, borderline hypertensives, and normotensives. They found high renin hypertensives to have suppressed hostility and higher levels of unexpressed anger compared to normals. These behavior patterns were associated with an increased sympathetic activity in this subgroup.

The present study confirms the inwardly angry, anxious, and slightly depressed ambience of hypertensives. It is possible that our sample was a special set of patient volunteers for hospitalization and tests and were thus unrepresentative of the general hypertensive population. But they exhibited normal noradrenergic and adrenergic responses to physical and mental stresses. Perhaps the resting sympathetic tone in these patients can be reduced by interventions that diffuse their abnormal psychodynamics and thereby lower BP.

Acknowledgments

We gratefully acknowledge the assistance of Joan Niemeyer, R.N., and the Clinical Research Center nursing staff, the help of Olivia Ramos with the computer evaluation, and the technical assistance of Daantje Meyer.

References

Anxiety, anger, and neurogenic tone at rest and in stress in patients with primary hypertension.

P Sullivan, S Schoentgen, V DeQuattro, W Procci, D Levine, J Van der Meulen and J Bornheimer

doi: 10.1161/01.HYP.3.6_Pt_2.II-119

*Hypertension* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1981 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/3/6_Pt_2/II-119

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/