Anger, anxiety, guilt and increased basal and stress-induced neurogenic tone: causes or effects in primary hypertension?


Department of Medicine, White Memorial Medical Center, and the Hypertension Service, Department of Medicine, and the Department of Psychiatry and Neurology, University of Southern California School of Medicine, Los Angeles, California, U.S.A.

Summary

1. Basal plasma and spinal fluid noradrenaline were increased in patients with primary hypertension and phaeochromocytoma compared with normotensive patients (P < 0.01).

2. Patients with primary hypertension had more anger (P < 0.01), anxiety (P < 0.01) and guilt (P < 0.05) than normotensive patients or patients with phaeochromocytoma.

3. The responses of noradrenaline and adrenaline concentrations were similar after mental and isometric stress in primary hypertensive and normotensive subjects.

4. However, after mental stress and isometric exercise there were increased responses of plasma noradrenaline and systolic blood pressure respectively, in patients with high anxiety and anger compared with those below the 50th percentile (P < 0.05).

5. Increased central and peripheral neurogenic tone at rest and after stress in association with increased anxiety and suppressed anger appear to be pathogenic factors in some patients with primary hypertension and may not be a result of the blood pressure elevation.

Key words: adrenaline, anger, noradrenaline, phaeochromocytoma, primary hypertension, psychology.

Abbreviation: IHE, isometric handgrip exercise.

Introduction

Neurogenic mechanisms have long been implicated in the pathogenesis of primary hypertension [1]. Suppressed anger was an attribute characteristic of young male patients with borderline hypertension who had biochemical indices of enhanced sympathetic tone [2]. The present study was designed to determine the relationship of psychological and neurogenic features to the blood pressure elevation of patients with primary hypertension at rest and during stress. In the attempt to define further a cause or effect role, these features were compared in patients with proven neurogenic hypertension due to phaeochromocytoma.

Methods

We performed studies in six patients with phaeochromocytoma, aged 42 ± 11 years, 15 patients with primary hypertension, aged 37 ± 11 years (means ± SEM) whose average blood pressure exceeded 140/90 mmHg on three occasions and 20 normotensive volunteers, aged 36 ± 8 years. None of the patients had cardiovascular or renal complications of their hypertension or had received antihypertensive medication within 3 weeks of the studies. Of those with phaeochromocytoma, three were receiving phenoxybenzamine. All patients signed an informed consent form which was approved by the Institutional Review Committee, after having been apprised of the nature of the study and its attendant potential risks. They were admitted to the Clinical Research Center of the Los Angeles County-USC Medical Center and were given a constant diet containing 100 mol of Na+ and 80 mmol of K+/day. Both patients and volunteers (studied in a similar manner but as outpatients) were fasted overnight.

Personality profiles were obtained 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 [3], the Spielberger State–Trait Anxiety Inventory [4], a modified and expanded version of an Anger-In/Anger-Out scale used by Harburg et al. [5] and the Buss-Durkee Hostility Inventory [6]. The psychological instrument was validated by clinical interviews with a psychiatrist.

Blood pressure and pulse rate were measured and venous blood was taken from an indwelling needle on the morning of day 2 after sitting for 30 min, and again at the end of 3 min of isometric handgrip exercise (IHE). IHE consisted of a workload of 33% of maximum voluntary contractions for 3 min. On day 3, cerebrospinal fluid noradrenaline was measured in 19 patients with primary hypertension (37 ± 3 years), 15 of whom had stress and psychological testing. Spinal fluid and plasma noradrenaline was measured in samples taken after 60 min supine and values were compared with those in a group of 11 normotensive patients with minor neurological disorders requiring lumbar puncture and who gave informed consent, three of whom had the IHE, mental stress and psychological evaluations. On day 4, the stress comprised 10 min of serial subtraction of numbers enforced by a metronome [7]. Measurements and blood were taken during the last 2 min of the serial subtraction. Noradrenaline and adrenaline were measured by the radioenzymatic assay of Peuler & Johnson [8]. Urinary sodium was measured by flame photometry. The questionnaires were scored by computer and the responses of the hypertensive patients compared with those of normotensive subjects using Student's t-test and chi-squared analysis.

Results

The arterial blood pressure of the patients with primary hypertension was 153 ± 15/104 ± 9 and 144 ± 51/96 ± 13 mmHg before IHE and mental stress respectively (means ± SEM). The values for normotensive subjects were 109 ± 12/73 ± 11 and 104 ± 12/70 ± 10 mmHg. Isometric stress produced significant increments of systolic and diastolic blood pressure of 5–10% and of pulse rate of 8–15% and were of similar magnitude for both groups (P < 0-01). Mental stress produced similar responses in the normotensive subjects (P < 0-01). However, heart rate (P < 0-01) and plasma adrenaline (P < 0-01) increased after mental stress in hypertensive patients without changes in blood pressure. The difference in systolic pressure response between the two groups after mental stress was significant (P < 0-01).

Plasma noradrenaline levels before IHE and mental stress were 50% greater in the primary hypertensive patients than in the normotensive subjects (P < 0-05, P < 0-05). Pre-stress levels of adrenaline of the hypertensive patients were not significantly different from those of the normotensive subjects. Plasma noradrenaline increased approximately 33% in response to IHE in both groups (P < 0-01). There was a significant increase of adrenaline in the hypertensive patients (80%) (P < 0-05) but that in the normotensive subjects was not significant. There was a 50% increment in adrenaline, but no significant change of noradrenaline in the response to mental stress in both groups (P < 0-05).

The prevalence of suppressed anger was increased in primary hypertension (P < 0-05), as were the scores for anxiety (P < 0-01), depression (P < 0-05) and guilt (P < 0-05) (Fig. 1). There were significant positive correlations of anxiety trait with systolic and diastolic blood pressures and with plasma noradrenaline (all P < 0-05). Primary hypertensive patients with anxiety scores above the 50th percentile had increased noradrenaline and systolic blood pressure responses to mental stress and IHE compared with primary hypertensive patients with lower anxiety scores (both P < 0-05). Furthermore, subjects with the combination of increased anxiety scores and suppressed anger had an enhanced increase of their systolic pressure after IHE (P < 0-05). Cerebrospinal fluid noradrenaline was 86% greater in the primary hypertensive patients when compared with normotensive subjects (329.4 ± 22.3 vs 177 ± 22.6 ng/l; P < 0-001 (Fig. 1).

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 blood pressures (r = 0-37, P < 0-05) and with plasma noradrenaline (r = 0-38, P < 0-05).

Discussion

Plasma noradrenaline was increased supine (P < 0-01) and sitting (P < 0-01) in primary hypertension compared with values in normotensive subjects.

The pressor responses of the primary hypertensive patients to IHE were similar to those of untreated hypertensive patients and normotensive subjects reported previously [9–11]. The changes
Psychology and neurogenic tone in hypertension

Cerebrospinal fluid (CSF) noradrenaline (supine) in normotensive subjects (NT), primary hypertensive patients (PH) and patients with phaeochromocytoma (PHAEO), with the scores for anger, anxiety and guilt proneness in the same groups. Significance values (P) reflect comparisons between NT and PH and between PHAEO and PH and are shown above the histograms. N.S., Not significant.

We observed in plasma noradrenaline in both our groups after IHE were similar to those of others at 3 min [10, 11]. The responses of adrenaline in our subjects were of an intermediate magnitude compared with others [10, 11]. Our 'contrived' mental stress seemed inadequate, inasmuch as the pressor response in normotensive subjects was approximately one-half of that described previously [7]. However, our findings confirmed the pattern of response of adrenaline to psychological stress [12]. Psychological factors have been implicated in primary hypertension since the turn of the century [13, 14]. Dunbar described hypertensive patients as afraid to show anger, with an excessive desire to please [14]. Buss discussed the importance of suppressed rage in the aetiology of hypertension [15]. Harburg et al., in a study of young college males, found that anxiety and neuroticism levels correlated strongly with blood pressure lability [16]. Harburg et al. [5] also reported significant relationships between withheld anger and blood pressure levels. Esler performed psychometric testing of high and normal renin, young, male, borderline hypertensive patients and normotensive subjects. He found high renin hypertensive patients to have suppressed hostility and higher levels of unexpected anger compared with normal subjects. These behaviour patterns were associated with an increased sympathetic activity in this subgroup [2].

The present study confirms the inwardly angry, anxious and slightly depressed character of hypertensive patients. On the other hand, the patients with phaeochromocytoma with 'secondary' hypertension did not have these psychological features. The primary hypertensive patients exhibited normal responses of plasma noradrenaline and adrenaline to physical and mental stress despite increased resting central and peripheral sympathetic tone. In patients with abnormal psychodynamics, neural and pressor responses to stress were enhanced. Perhaps psychological evaluation such as autogenic training or methods which improve coping patterns can reduce central neurogenic tone and the blood pressure of some patients with primary hypertension.

Acknowledgments
Sponsored by NIH Grant no. HL24113 and Clinical Research Center Grant GCRC-RR-43. We gratefully acknowledge the assistance of Joan
Niemeyer, R.N., and the Clinical Research Center Nursing Staff, help with the computer evaluation by Olivia Ramos and the technical assistance of Daantje Meijer.

References


