Reduction in Drug Requirements for Hypertension by Means of a Cognitive-Behavioral Intervention

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The purpose of the present study was to test the effectiveness of a cognitive-behavioral intervention as an adjunctive treatment of hypertension. To qualify for the study, subjects had to have an unmedicated clinic diastolic blood pressure \(\geq 95\) mm Hg. After qualification, minimal drug requirements were established using a diuretic and a \(\beta\)-blocker to control blood pressure at \(\leq 90\) mm Hg. Subjects were then randomized into a 6-week cognitive-behavioral intervention or a measurements-only control group. After the treatment phase, medication levels were reduced in all subjects by means of a systematic stepdown procedure. Subjects were followed for 1 year after the stepdown was completed. Addition of the cognitive-behavioral intervention was twice as effective as the control procedure in reducing drug requirements. At 12-months follow-up, 73% of the treatment group were at lower levels of medication than at the time of randomization, compared to 35% in the control group. Moreover, 55% of the treatment group remained completely free of medication, compared to 30% of the control group, at the 12-month follow-up. The reductions in medication were associated with maintained controlled levels of clinic, ambulatory, and home blood pressure. The addition of a standardized and inexpensive group-administered cognitive-behavioral intervention to the drug treatment of hypertension is beneficial as an adjunctive treatment in reducing drug requirements for patients with hypertension, thereby reducing the costs and potential side effects of antihypertensive medications. © 1997 American Journal of Hypertension, Ltd. Am J Hypertens 1997;10:9–17

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Significant advances have been made in the use of relaxation and stress reduction as alternative or adjunctive methods of treating physical disorders. A foremost application has been in hypertension, for which hundreds of empirical studies have been published, including five metaanalyses that provide some support for the effectiveness of behavioral treatments for unmedicated hypertensive patients. In studies of combined drug/behavioral treatments, however, the evidence has been less conclusive. Studies reporting negative findings have generally included medicated patients with relatively low pretreatment blood pressure (BP). The lower the initial level of BP, the smaller the BP reduction obtained, whether by medications or by behavioral treatments. In such patients, a floor effect may oper-
ate such that further BP reductions with behavioral treatment are unlikely. Studies reporting positive findings have generally included subjects with relatively high pre-treatment BP. It is not known, however, whether these subjects accounted for the significant effects. BP reduction may be appropriate as an outcome measure only in populations selected for higher pretreatment BP in whom “floor effects” are thereby avoided. In medicated patients with relatively low pretreatment BP, medication reduction may be the more appropriate measure. The Fifth Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC V) discussed the benefits of weight reduction and increased moderation of dietary sodium and alcohol intake for reducing BP or the number and doses of medication needed to manage hypertension. Such lifestyle modifications may also reduce other risk factors for premature cardiovascular disease. The JNC V Report concluded that although stress has an effect on BP, the role of stress reduction in the treatment of hypertension was uncertain. Several studies suggest the potential utility of psychological treatments as an adjunct to pharmacotherapy and as a means of decreasing medication requirements, although methodological problems in these studies have precluded firm conclusions.

The purpose of the present study was to evaluate the potential benefits of a cognitive-behavioral stress reduction intervention as an adjunctive treatment of medicated patients with hypertension. We hypothesized that the addition of a behavioral component to drug therapy of hypertension would lead to a greater reduction in the antihypertensive medication level required to maintain BP at controlled levels, as compared to a drug therapy only control condition. The study was conducted in patients with mild-to-moderate hypertension (Stage 1 and Stage 2 patients according to JNC V). The research design incorporated several critical key features: pretreatment evaluation of subjects’ unmedicated blood pressure, initial determination prior to treatment of minimal drug requirements to achieve BP control, use of the same types of medications for all subjects, systematic posttreatment evaluation of drug reduction in both control and treatment subjects by means of a stepdown procedure, and a 1 year post-treatment follow-up. We chose to use a diuretic and a β-blocker in the drug treatment of patients because these two classes of drugs have been shown to reduce cardiovascular morbidity and mortality in controlled trials and are commonly used and preferred as initial therapy for hypertension. Changes in drug requirements both in treatment and control subjects during the study followed strict rules. The research also incorporated multiple assessments of clinic, home, and ambulatory BP and of psychosocial factors and quality of life.

**METHODS**

**Subjects** The subjects were 39 patients with a history of mild-to-moderate hypertension. Only subjects with primary hypertension were accepted into the study. This was determined by history and a physical examination that included fundoscopy, 12-lead electrocardiography, urinalysis, hematology, and serum chemistry. Exclusion criteria were as follows: secondary hypertension; hypertensive complications (left ventricular hypertrophy, proteinuria, retinopathy); history of cardiovascular disorders, stroke, diabetes mellitus, asthma, epilepsy, obstructive valvular disease, malignant hypertension, renal disease, or hepatic disease; pregnancy; severe obesity; drug or alcohol abuse; current medical or psychiatric treatment; or any contraindications to the administration of the study medications. The physical examination was repeated at the 12-month follow-up, including a biochemical profile. No adverse effects of the study medications, such as increased levels of cholesterol, were observed. Subjects had to be willing to carry out all the procedures and to commit themselves to a large number of required clinic visits. The research was approved by the UCLA Human Subjects Protection Committee and all subjects gave their informed consent. The characteristics of the 39 final participants are given in Table 1. Treatment and control groups differed significantly only in age (t test, P < .02).

Subjects were recruited by means of advertisements in local and community newspapers and by referral from physicians. A stated goal of the project was to determine whether a behavioral intervention would be more effective than a control procedure in achieving reduced drug requirements. All subjects (treatment and control) were told that participation in the various procedures of the program, including home and ambulatory blood pressure monitoring, could be beneficial in the management of their hypertension and in lowering the amount of drugs needed to control their BP. Many subjects reported that their participation was motivated by a desire to reduce or stop medications entirely. At intake into the study, 26% of the subjects were not taking any medications, and the remaining subjects were taking different single or combined antihypertensive medications.

The design and sequence of procedures and measurements is outlined in Figure 1. To qualify for participation in the study, subjects had to have an unmedicated diastolic blood pressure (DBP) between 95 and 110 mm Hg. Volunteers already taking antihypertensive medications were slowly weaned off their current medications prior to evaluation of their eligibility for the study. After being completely withdrawn, they were followed over a 4 to 6 week period. The criterion for entry into the study was based on DBP averaged over three visits during a 2 to 4 week period. About 15% of the volunteer subjects did not qualify in this time period. Unmedicated qualification blood pressure levels of the 39 subjects are given in Table 1. According to JNC V criteria, out of the 22 treatment subjects, 17 had Stage 1 and 5 had Stage 2 hypertension. The respective numbers were 15 and 2 in the control group.
After qualification, a minimal drug requirement was established for each subject to achieve BP control at DBP ≤ 90 mm Hg. Clinic BP was the sole determinant of all changes in medication during this phase and all other phases of the study. All patients were given the same sequence of drugs in five steps starting with diuretic (Dyazide, SmithKline Beecham, Philadelphia, 25 mg hydrochlorothiazide and 50 mg triamterene) followed by addition of the cardioselective β-blocker atenolol from 25 mg to 100 mg in 25 mg increments as required. At each step, BP was assessed over three visits over 2 to 3 weeks until the DBP criterion was achieved. The medication level at which BP control was achieved defined the minimal drug requirement.

Subjects were then randomized into treatment and control groups. During the treatment phase, which fol-

**FIGURE 1.*** Study protocol indicating major phases and procedures of study.
followed over a 6 week period, treatment subjects participated in a cognitive-behavioral treatment program in weekly 1.5-h group sessions and a brief clinical and BP evaluation. The treatment sessions were conducted by a licensed clinical psychologist (MEO). To assure a comparable frequency of contact with the project staff, control subjects also visited the clinic at the same times as treatment subjects but mainly for the clinical and BP evaluation, which was done by a nurse practitioner. With each subject, the nurse discussed adherence to medication and the daily home blood pressure recording, as well as any recent changes in the subject’s life. No changes in medication were made in this phase of the study.

Following the 6-week treatment phase, all subjects (treatment and control) participated in a drug stepdown procedure in which medication level was reduced by one step at a time. For subjects on combined atenolol and diuretic, the atenolol dose was reduced by 25 mg at a time. For subjects on diuretic only, medication was completely withdrawn. This process was begun as long as BP was stable and still under control (DBP < 90 mm Hg) at the end of the 6 week treatment/control period. After each stepdown of medication, BP was assessed over three visits in a 2 to 3 week period. Stepdow was considered completed at the lowest medication step at which DBP remained ≤ 90 mm Hg, based on the three-visit mean value. For subjects who were able to be stepped down to no medication, DBP had to remain < 95 mm Hg DBP.

The follow-up period was initiated at the completion of the stepdown procedure and continued for 1 year. During follow-up, all subjects were seen for a BP assessment and brief check-up at 1-month intervals for the first 3 months and then at 3-month intervals for the remaining 9 months. Treatment subjects also participated in a brief “booster” session in which they discussed problems and reviewed their continuing adherence to the various procedures of the intervention. For all subjects during these follow-up visits, whenever the DBP (mean of three readings) was above criterion, two more visits were scheduled to determine if medication had to be stepped up. If so, the next step of medication was added, and a new 3-visit evaluation commenced. The procedure was continued until control was achieved at DBP ≤ 90 mm Hg. Medication adjustments continued as needed throughout the remaining followup period, following strict rules that were identical for treatment and control subjects.

Figure 1 also indicates the periodic psychosocial and quality of life assessments and the times at which ambulatory blood pressure monitoring was done. Throughout the program, all subjects were asked to record their own BP at home on a daily basis.

**Clinic BP** To minimize bias, clinic BP was obtained with a random-zero sphygmomanometer (Hawksley & Sons, Lancing, England). In each evaluation, three successive readings were taken at 2-min intervals after a 10-min rest period. Means of the three readings of a given evaluation were used in the analyses, usually combined with the means obtained on two additional visits for each phase of the study.

**Ambulatory BP Monitoring (ABPM)** ABPM was done only at certain phases of the program (see Figure 1) using the Accutracker II (Suntech Medical Instruments, Raleigh, NC). Previous research has established the validity and reliability of this monitoring device. The device was programmed to operate three times an hour during waking hours and hourly during sleep for each 24-h recording. All ambulatory recordings were made on a weekday. Reported in the analyses are mean values for awake and sleep periods. Procedures for recording and elimination of artifacts are described elsewhere.

**Home BP Recording** Subjects were instructed by the nurse on how to take their own BP using an auscultatory sphygmomanometer (Propper Model #214011, Propper Manufacturing, Long Island City, NY) following American Heart Association guidelines. A T-connector and a teaching stethoscope were used to check their procedures and accuracy. Subjects were asked to record their BP three times on three occasions at home during the day (on awakening, before dinner, and at bedtime). For the major phases of the study, we used the mean of the readings made on the three days parallel to the three clinic days used for the clinic BP assessments. For the follow-up visits, we used three consecutive days nearest to the clinic visit of the particular follow-up visit.

**Psychosocial and Quality of Life Assessments** At various phases of the study (see Figure 1), all subjects took a battery of tests including (a) the Buss-Durkee Hostility Inventory (BDHI), a 75-item true-false questionnaire designed to provide a total hostility score and scores on assault, indirect hostility, resentment, suspicion, irritability, negativism, guilt, and verbal hostility subscales; (b) the Marlow-Crowne Social Desirability (MC) scale, used as a measure of defensiveness (subjects scoring high on this scale typically score low on scales of negative emotions, eg, hostility, anxiety); (c) the Taylor Manifest Anxiety Scale, used as a measure of anxiety; (d) the State and Trait forms of the Spielberger State-Trait Anxiety Inventory, used as measures of state and trait anxiety; (e) the Beck Depression Inventory, used as a measure of depression. These tests were selected as standardized assessments of psychological characteristics examined in quality of life studies and also because of their empirical association with hypertension or with blood pressure variations in healthy subjects. The test battery included questionnaires to assess work performance, sleep problems, physical
symptoms and drug side effects, and sexual function. Changes in health habits were also assessed: use of caffeine, alcohol, and salt, amount of regular exercise, and leisure/recreational activity. Weight was measured, and a neuropsychological test of short-term memory was administered on each occasion.26

Cognitive-Behavioral Intervention Subjects in the treatment group participated in six weekly 1.5-h sessions in groups of two to four and also in 30-min “booster” sessions at each follow-up period. The sessions were designed to cover a wide variety of cognitive and behavioral methods designed to facilitate stress reduction, previously shown to reduce BP acutely or to be effective in behavioral intervention studies27 (Table 2). Subjects were instructed to experiment with each method and to focus on those procedures that matched their lifestyle requirements. A major component of the program was progressive muscle relaxation training. Subjects were provided with relaxation tapes to practice once a day at home. They were also given a digital temperature biofeedback device for home practice in relaxation. Effective methods of coping with stress and emotional reactions were emphasized using cognitive therapy techniques. Each subject was given a manual of procedures describing the basic concepts and methods of stress management and laying out the various exercises to be done at home over the 6-week period. The manual provided a rationale for the intervention in general and for each specific procedure. Questionnaires were used at the beginning of each session to assess adherence to the home practice and the use of the various treatment methods. Subjects reported that they tended to emphasize two or three procedures that they preferred and found useful.

Statistical Analysis In the analysis of medication level, medication steps were assigned values as follows: 0 = none, 1 = diuretic only, 2 = diuretic plus 25 mg atenolol, 3 = diuretic plus 50 mg atenolol, 4 = diuretic plus 75 mg atenolol, and 5 = diuretic plus 100 mg atenolol. Between- and within-group t tests were used for selective comparisons of medication level. Changes in medication level were analyzed by analysis of variance for repeated measures over selected phases of the study, comparing treatment and control conditions. Age was used as a covariate in these analyses. Significant interactions were further examined by t test. Medication reduction was also examined by making counts of subjects who showed a change of medication level over selected study phases, comparing treatment and control subjects. Fisher’s Exact Test was used to test the significance of differences in these counts.

Comparable analyses of variance were made of changes in clinic, home, and ambulatory BP and in the various psychosocial and quality of life measures. To determine predictors of medication reduction, Pearson correlations were computed between changes in medication requirements and changes in psychosocial and quality of life measures from randomization to the 12-month follow-up. The role of demographic and other variables as predictors of medication reduction was similarly examined by Pearson correlations.

An α-level of .05 was used to define statistical significance.

RESULTS

Medication Levels The mean medication level per phase is shown in Figure 2. At the time of randomization, medication levels did not differ between the treatment and the control group. Both groups showed significant and comparable reductions in medication at stepdown completion (P < .001). Analysis of variance of medication level indicated a significant interaction between group (treatment versus control) over the five phases of the study (P = .018), starting with stepdown completion. Control subjects tended to return to randomization levels beginning with the 3-month follow-up, whereas treatment subjects tended to maintain their gains for the remainder of the study (Figure 2). Medication level was significantly lower in the treatment than in the control group at all follow-up phases.

Comparing stepdown completion and the 12-month follow-up, 47% of the control subjects increased their level of medication compared to 14% in the treatment group (P = .033). Comparing medication levels at randomization versus the 12-month follow-up, 73% of the treatment subjects had lower levels at the end of the study, compared to 35% of the controls (P = .026). These data indicate that the behavioral intervention resulted in significantly greater maintenance of medication reduction in the treatment group than in the control group. Fifty-five percent of treatment subjects were not taking any medications by the end of the 1-year follow-up period compared to 30% in the control group.

### TABLE 2. COMPONENTS OF COGNITIVE-BEHAVIORAL INTERVENTION

| 1. Progressive muscle relaxation training with daily home practice. |
| 2. Cue-controlled relaxation and imagery. |
| 3. Autogenic training. |
| 4. Assertiveness training. |
| 5. Digital temperature biofeedback training with home practice. |
| 6. Time management. |
| 7. Deep diaphragmatic breathing. |
| 10. Manual describing general rationale and explanation of methods, session-by-session topics and exercises, and home practice assignments. |
Clinic BP  Mean clinic BP values for each major phase are shown in Figure 2. A significant reduction in both SBP and DBP ($P < .001$) occurred from unmedicated to randomization phases. Analysis of variance of clinic SBP and DBP for the remaining phases showed no significant main effects or interactions. Despite the reduction or withdrawal of medication in the subjects, comparing randomization and subsequent phases, BP levels were maintained at controlled levels in both groups. Of special significance is the fact that BP levels did not differ between groups during the follow-up phases despite the fact that significantly greater reductions in medication were achieved in the treatment condition.
Ambulatory BP  Significant reductions in awake SBP and DBP (P < .001) were obtained after medication requirements were established (unmedicated to randomization phase). No other significant differences in ambulatory SBP and DBP over phases or between groups were revealed by analysis of variance. Awake data are shown in Figure 2. The pattern of results was comparable for both waking and sleep ambulatory BP. These data are in accordance with the findings for clinic BP.

Home BP  The BP data recorded by the subjects at home revealed a comparable pattern of findings comparable to the clinic and the ambulatory data. A significant reduction in home SBP and DBP (P < .001) was shown from unmedicated to randomized. Analysis of variance of the remaining phases showed no significant main effects or interactions.

Summarizing the BP findings, clinic BP showed maintained control despite changes in drug requirements over the course of the study. Moreover, BP control was comparable in both treatment and control groups, even through the treatment group had a significantly greater reduction in drug requirements and a higher percentage of subjects who were free of medication than in the control group. The clinic BP findings are supported by parallel findings for ambulatory and home BP.

Psychosocial and Quality of Life Changes  Reports of quality of life at randomization, 6-month follow-up, and 12-month follow-up periods were compared for the treatment and control groups. No significant main effects or interactions were obtained for these variables (work performance, sleep problems, physical symptoms and drug side effects, and sexual function). Analyses of the personality test scores (hostility, anxiety, depression, etc) also yielded no significant effects. No significant changes were shown for health habits or body mass index over the course of the study. Finally, out of the eight measures of short-term memory, only one (short term retrieval) showed an effect for phase (P = .009), based on an improvement in this measure over the course of the study that did not differ between treatment and control subjects.

Predictors of Drug Reduction  The greater the reduction in hostility (total BDHI score) and in defensiveness (MC scale), the greater the reduction in medication (P = .035). These effects were independent of treatment condition. Other changes in psychosocial, quality of life, and health habit variables, including body mass index, were not associated with degree of reduction. Variables such as age, sex, race, education, and years of hypertension were not associated with medication reduction.

DISCUSSION  

Addition of a cognitive-behavioral intervention to the drug treatment of mild-to-moderate (Stage 1 to 2) hypertension proved effective in reducing drug requirements. The intervention was about twice as effective as a control procedure, which also involved drug treatment. In both conditions, there was a comparable degree of contact between the subjects and clinical staff. The reductions in medication occurred in subjects who had hypertensive levels of blood pressure (unmedicated) on intake into the study. At lower levels of medication, they were nonetheless able to maintain controlled levels of blood pressure, whether assessed in the clinic, at home, or over the course of 24 h by means of ambulatory monitoring.

The significance of the medication reduction can be viewed in relation to the pattern of blood pressure change associated with the program. Consider the 12 patients in the treatment group who were not taking any medications at the 12-month follow-up. At the time of initial qualification (at which time they were also unmedicated), their clinic blood pressure averaged 145/97 mm Hg. At the time of the 12-month follow-up, when they were again free of medications, their clinic blood pressure averaged 137/88 mm Hg. The reduction of 8/9 mm Hg can be viewed as an index of the blood pressure lowering effect of the program in these subjects. For the five control subjects who benefited from participation in the project and who were free of medication at the 12-month follow-up, the results were similar with an 8/11 mm Hg average reduction in blood pressure. Results of the present study are consistent with the findings reported by Glasgow, Engel, and D’Lugoff,16 which represents the best example of a similar attempt to determine the extent to which a behavioral intervention might supplement or replace antihypertensive drug treatment. However, the Glasgow et al study did not use a posttreatment stepdown procedure for control subjects, as was done in the present study.

To what can we attribute the apparent benefits obtained in the present study as compared to earlier evaluations of combined drug and behavioral treatments? One possibility is the quality of the present intervention itself, which included a variety of methods of stress reduction as well as relaxation and biofeedback. Furthermore, subjects were able to concentrate on those techniques they found most appropriate to their personal style or life circumstances. Another possibility is the close, personal, and frequent contact between each subject and a member of the project staff, who was generally the same person throughout the study. This probably was a factor in the reduction of drug requirements achieved by control subjects, in addition to self-monitoring of blood pressure and greater attention to their hypertension. Last is the conceptualization and design of the present study, in particular the use of medication reduction rather than blood pressure reduction as the primary outcome measure.
The question may be raised as to what the treatment subjects learned. This study employed a multilevel treatment program in which each subject focused on specific components. It is not possible to determine which interventions were most effective. The paucity of results using various psychosocial questionnaires suggest that these methods of assessment were not sensitive to the critical processes of change. We can speculate that the cognitive-behavioral treatment helped subjects learn ways of reducing or modifying their reactions to situations, which in turn served to reduce their blood pressure and hence need for medication. This learning was probably facilitated by an increase in subjects’ attention to their blood pressure and its day-by-day fluctuations. The stress reduction methods used in this study may be thought of as the learning of different ways of reducing one’s own blood pressure or keeping it from increasing, facilitated by an increased awareness of changes in one’s blood pressure and one’s characteristic ways of responding to stress. The careful titration of drugs at the beginning of the program and in the posttreatment stepdown process may have also brought about a greater sensitivity to factors leading to variations in one’s blood pressure. This process may have facilitated medication reduction, which may account for the greater reduction in our control group than that seen by Glasgow et al., who did not systematically stepdown their control subjects after the treatment phase was concluded. In the case of treatment subjects, this process was facilitated by learning various methods of reducing blood pressure and of coping with stress.

Independent of experimental group, reductions in hostility and defensiveness were found to be associated with medication reduction. As noted earlier, the presence of these factors has been related to increased levels of blood pressure in normotensive and hypertensive individuals. Learning more effective ways of handling and acknowledging feelings of anger and hostility may be an especially valuable component of behavioral treatment programs.

The nurse practitioner who measured blood pressure in the clinic was not blind as to which group (treatment or control) the subject was assigned. This raises the question of possible bias in the determination of medication adjustments, which depended on clinic blood pressure. To minimize bias, blood pressure was assessed with a random-zero sphygmomanometer. Medication adjustments were based on mean diastolic blood pressure over three visits, three measurements per visit. Clinic assessments were consistent with measurements taken by subjects at home, and they were also consistent with automatic determinations of blood pressure made in the periodic ambulatory recordings. For example, mean values of waking and sleeping pressure were almost identical for the treatment and control groups at the time of the 12-month follow-up, even though the groups differed significantly in their medication levels at that time. Moreover, the nurse practitioner was blind as to the ambulatory measurements. Thus, the adjustments in medication cannot simply be attributed to potential experimenter bias. Subjects’ expectations about the program may have also been a factor in the findings. Both treatment and control subjects were told that their participation in the program could help them reduce their blood pressure, such as through knowledge of daily variations in their pressure from the home readings, and all subjects had an equivalent number of contacts with project staff.

The paucity of psychosocial and quality of life findings related to the obtained drug reduction achieved by many subjects deserves further comment. The present study employed either diuretic or diuretic combined with a β-blocker. Neither drug has been associated with major negative quality of life findings, with the exception of sexual dysfunction which is associated with diuretics in men. Moreover, major uncertainties remain in attempts to arrive at definite conclusions about the quality of life consequences of antihypertensive medications. A recent metaanalysis could not identify negative effects with treatment. Another important consideration is the fact that in the present study minimal drug requirements were established and individualized for each patient rather than standardized as in usual clinical drug trials. This may have reduced the likelihood of negative impact of the drugs on quality of life.

In conclusion, the addition of a standardized and inexpensive group-administered cognitive-behavioral intervention appears to be beneficial as an adjunct treatment in reducing drug requirements or as an alternative to drug treatment for some patients with high blood pressure. In an era of increasing attention to treatment alternatives and rising health care costs, interventions of this kind should have their place in the treatment of hypertension and possibly in other disorders. They also may be beneficial for some patients in minimizing potential adverse side effects of medications and enhancing quality of life. Monitoring one’s own pressure regularly is one simple and inexpensive method of increasing awareness of changes in one’s own blood pressure and thereby facilitating greater control. Teaching people how to recognize and cope with stress as well as the use of simple relaxation and biofeedback methods may allow them to put into practice those methods they find most useful and beneficial. Cognitive-behavioral interventions can facilitate continued blood pressure control as less medication is required or medication is no longer needed. The present study was carried out in subjects with mild-to-moderate hypertension, selected according to strict eligibility criteria. Generalizability of the find-
ings to other hypertensive subjects remains to be determined.

REFERENCES


