REVIEW ARTICLE

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Effects of Exercise, Diet and Weight Loss on High Blood Pressure

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Abstract

High blood pressure (BP) is a major health problem in the US, affecting more than 50 million people. Although high BP is among the most common reasons for outpatient visits, BP control is often inadequate. It is well established that BP can be lowered pharmacologically in hypertensive individuals; however, anti-hypertensive medications are not effective for everyone, and may be costly and result in adverse effects that impair quality of life and reduce adherence. Moreover, abnormalities associated with high BP, such as insulin resistance and hyperlipidaemia, may persist or may even be exacerbated by some anti-hypertensive medications. Consequently, there has been a great deal of interest in the development and application of behavioural interventions in the management of high BP.

The main behavioural interventions that are recommended to reduce BP are exercise and the Dietary Approaches to Stop Hypertension (DASH) diet. Weight loss is also recommended for BP reduction in overweight individuals. Exercise alone is associated with reductions of approximately 3.5 and 2.0mm Hg in systolic (SBP) and diastolic blood pressure (DBP), respectively. Patients fed a DASH diet (a diet high in low-fat dairy products and fibre, including fruits and vegetables) had reductions in SBP and DBP of 5.5 and 3.0mm Hg, respectively, compared with those consuming a standard US diet. Reductions of approximately 8.5mm Hg SBP and 6.5mm Hg DBP accompany weight loss of 8kg. In overweight hypertensive patients, a combined exercise and weight-loss intervention has been shown to decrease SBP and DBP by 12.5 and 7.9mm Hg, respectively.

There is evidence to suggest that these decreases in BP are associated with improvements in left ventricular structure and function, and peripheral vascular health. Both exercise training and weight loss have been shown to decrease left ventricular mass and wall thickness, reduce arterial stiffness and improve endothelial function. These data support the role of behavioural interventions in the treatment of patients with elevations in BP.

1. Risk and Cost of High Blood Pressure

Cardiovascular disease is the leading cause of death in the US, with an estimated economic cost of more than $US350 billion (2003 values) for which high blood pressure (BP) is a major modifiable risk factor. Hypertension is defined as chronically elevated high BP, with systolic blood pressure (SBP) of 140mm Hg or greater, diastolic blood pressure (DBP) of 90mm Hg or greater, or taking anti-hypertensive medication.[1] BP in excess of 140/90mm Hg is further categorised in terms of severity of hypertension, defined as stage 1 (140–159/90–99mm Hg) or stage 2 (≥160/100mm Hg). Although BP less than 140/90mm Hg was once considered normal, the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)[1] now includes the category of 'pre-hypertension', defined as the pressure range 120–139/80–89mm Hg. Only pressures below 120/80mm Hg are considered optimal. One out of every four adult Americans currently has high BP, and this number is projected to increase over the next decade. The morbidity and mortality associated with hypertension are also substantial,[2] with prospective observational studies estimating that a 5–6mm Hg DBP elevation predicts an approximate 35–40% increased risk of stroke and a 20–25% increased risk of ischaemic heart disease (IHD).[3,4] Stroke-related mortality is effectively reduced following anti-hypertensive drug treatment; however, reductions in IHD-related mortality have been less consistently demonstrated in treatment trials.[3,4] The relatively modest reduction in IHD-related death observed in clinical trials emphasises the need for alternative treatments such as lifestyle changes of diet and exercise. In addition to producing reductions in BP, these lifestyle changes also improve other comorbid risk factors, such as hyperinsulinaemia and dyslipidaemia.[5-8]

2. Clinical Consequences of Hypertension

Although hypertension is defined by elevation of arterial BP, its clinical significance is derived from morbid events affecting the heart, brain and kidneys. Complications such as myocardial infarction and stroke are not directly due to elevated BP, but to the resulting structural changes in the heart and blood vessels. One of the structural consequences of hypertension, left ventricular hypertrophy (LVH), is the strongest known predictor, other than advancing age, of cardiovascular morbidity and mortality. Increased left ventricular (LV) mass predicts these clinical outcomes both in individuals with hypertension[9] and in healthy individuals,[10] independent of other conventional risk factors. The geometric pattern of hypertrophy is also of prognostic significance. Patients with concentric remodelling – an increase in the ratio of wall thickness to chamber dimension but normal LV mass – have a cardiovascular risk intermediate between those with normal LV structure and those with concentric hypertrophy. It has been shown that hypertrophy is reversible with regression being associated with a reduction in cardiovascular risk.[11]

3. Effects of Exercise on Blood Pressure

The value of physical activity and aerobic exercise in lowering BP has been the subject of numerous reviews.[12-20] The majority of studies have been cross-sectional and consistently demonstrate an association between higher levels of fitness and lower BP. The strengths of these studies lie in their large sample sizes, the diversity of patient populations studied, and in the consistency of results despite widely differing methodologies. There also have been several large longitudinal studies that have demonstrated a positive association between physical fitness and lower BP, including studies of 7685

University of Pennsylvania alumni[21] and 14 998 Harvard alumni.[22,23] In both studies, the prevalence of hypertension was inversely related to physical activity. A third longitudinal study investigated 4820 men and 1219 women who were normotensive at the time of self-referral to a preventive medicine clinic.[24] The relative risk of developing future hypertension in the low fitness subjects, compared with the high fitness subjects, was 1.52 (confidence interval 1.08, 2.15). This association was present after controlling for age, body mass index, baseline BP and follow-up interval.

The major randomised trials of exercise in patients with hypertension have been reviewed previously.[14,19] Despite claims by a number of highly respected organisations such as the American College of Sports Medicine[12] that exercise will produce a 10mm Hg reduction in both SBP and DBP, results from well controlled studies offer more conservative estimates. Results from randomised trials have been inconsistent and certainly the magnitude of effects are much smaller. Moreover, most of the studies have been limited because of high dropout rates, unplanned crossover, imprecise measurement of BP or aerobic fitness, or failure to precisely measure other potential confounders (e.g. bodyweight) and few studies included adequate numbers of women. Better designed studies with greater methodological rigour generally demonstrate smaller exercise-related BP reductions than studies with less rigorous controls and recent meta-analyses demonstrated more modest reductions. One meta-analysis[16] suggested that a 2% reduction in resting SBP and a 1% reduction in DBP was more likely, while a second[25] reported an average BP reduction of 3.8/2.5mm Hg based upon 54 studies involving 2419 participants. It has also been suggested that moderate-intensity exercise (<70% maximal effort) is equivalent to, and may be potentially even better than high-intensity exercise (>70% maximal effort) in reducing high BP.[26]

4. Dietary Approaches to Blood Pressure Reduction

A recent review of behavioural interventions in the treatment of hypertension including studies of dietary factors such as: alcohol restriction, sodium restriction, and potassium, magnesium and calcium supplementation, concluded that a healthy eating pattern, as exemplified by the Dietary Approaches to Stop Hypertension (DASH) diet, was the optimal dietary approach to BP reduction.[14]

Generally, it has been found that reducing alcohol consumption is associated with a lowering of BP, particularly in heavy drinkers. A recent review of the literature[27] found a direct link between chronic alcohol intake (≥30–60 g/day) and elevated BP. It was estimated that, in heavy drinkers, a reduction of 10 g/day of alcohol would result in a decrease in SBP of 1–2mm Hg and in DBP of 1mm Hg. In addition to raising BP, excessive alcohol consumption also can lead to resistance to antiphypertensive therapy, thus further increasing BP.[28] It should be noted that for patients with high levels of alcohol consumption, reductions in BP are seen several days after withdrawal of alcohol, as the initial stages of withdrawal lead to an acute increase in BP.[29]

Data from both clinical trials and cross-sectional epidemiological studies have demonstrated an association between dietary sodium intake and elevated BP. One review has estimated that a 50 mmol/day reduction in sodium intake, in people aged 50–59 years, was associated with a decrease in SBP of 7mm Hg in hypertensive patients and 5mm Hg in normotensive patients.[30] In general, however, short-term trials of sodium restriction have been associated with average reductions in SBP of 4.9mm Hg and in DBP of 2.6mm Hg.[31] However, the relationship between sodium and BP is influenced by individual differences in salt-sensitivity, where those people who are salt-resistant do not raise their BP when exposed to salt, but salt-sensitive individuals do exhibit an increase in BP.[32] As would be expected, the greatest benefits of sodium reduction are seen in those who are salt-sensitive.

Other minerals that have been assessed in relation to BP level are potassium, calcium and magnesium. Of the three, potassium has shown the most robust results with high dietary intake potentially protecting against the development of hypertension,[33] while a deficiency may increase BP.[34] A meta-analysis of 33 clinical trials found that potassium supplementation was associated with a reduction in SBP of 3mm Hg and DBP of 2mm Hg.[35] Reduced calcium intake has been associated with higher levels of BP in some, but not all, epidemio-

logical studies[1] and it is believed that its effects are synergistic with those of increased sodium intake.[36] A meta-analysis of 22 clinical trials found calcium supplementation to reduce SBP by 1.0mm Hg and DBP by 0.2mm Hg.[37] The overall effects of increased calcium on reduction in BP are minimal and at this time it is unclear which patients will benefit the most.[38] There is suggestive evidence that low dietary magnesium may be related to higher BP. A randomised crossover study of 60 hypertensive patients did find a significant, but small, reduction in BP following 8 weeks of magnesium supplementation.[39] Due to the small number of studies and the limited effects of magnesium on BP no substantive conclusion can be drawn at this time.

In addition to the studies of individual nutrients, whole diet approaches to controlling BP have been tested, the most recent of which is the DASH study. DASH was a National Heart, Lung, and Blood Institute-sponsored four-centre, randomised feeding trial designed to compare the effects of three dietary patterns on BP among 459 unmedicated persons with higher than optimal DBP or with stage 1 hypertension. The three dietary patterns included: (i) a 'control' diet reflecting what many Americans eat; (ii) a fruits and vegetables diet that was high in fruits and vegetables, but otherwise similar to the control diet; and (iii) a 'combination' diet (the DASH diet) that was high in fruits, vegetables, and low-fat dairy products with reduced total fat, saturated fat and cholesterol. Sodium content and bodyweight were kept constant through the entire study. The design of the DASH study is described in detail by Appel et al.,[40] and the study outcomes have been reported.[40-42] The main outcome for the DASH study was clinic BP. Compared with the control diet, the DASH diet reduced both SBP and DBP by 5.5 and 3.0mm Hg, respectively. BP was reduced by 11.4/5.5mm Hg among the 133 participants with stage 1 hypertension compared with the control diet; among the 326 participants without hypertension, the corresponding reduction was 3.5/2.1mm Hg.[40] Interestingly, the effects of the DASH diet, relative to the control diet, were greater for African Americans than for non-African Americans.[40]

The second DASH study[43] was also a controlled-feeding study designed to compare the effects of three levels of sodium intake and two dietary patterns on BP among unmedicated participants with stage I hypertension, in which 412 persons were enrolled. Participants were randomly assigned to a control diet typical of either the US intake or the DASH diet. Within their assigned diet, participants were fed 3 sodium levels (150, 100 and 50 mmol/day for a 2100 kcal diet) for 30 days each in a crossover design. At all levels of sodium intake SBP reduction was greater with the DASH diet than the control diet (–5.9, –5.0 and –2.2mm Hg for each of the three sodium levels). Reductions in sodium intake were associated with further decreases in SBP for both the DASH (3.0mm Hg reduction from 150 to 50 mmol/day sodium) and control (6.7mm Hg reduction from 150 to 50 mmol/day sodium) diets. It should be noted that in younger normotensive populations, the BP-lowering effects of sodium reduction in addition to changes in whole diet have been questioned.[44] The Trials of Hypertension Prevention study found that limiting sodium intake to current recommended levels was less effective than the DASH diet in reducing BP.[45] Thus, for the majority of people, salt intake alone may have relatively little influence on BP.[44]

As the DASH diet is effective for most segments of the population, including African Americans,[46] it is part of current national recommendations for the prevention and treatment of high BP (JNC 7).[1] It should be emphasised, however, that the DASH studies were 'feeding studies' in which patients received prepared food for the 2-month treatment programme, and the study was designed to assess the impact of diet, independent of weight loss. Although there are no known studies of just the DASH diet in a 'free-living' setting, the recent PREMIER study[47] assessed the effects of the DASH diet in combination with other lifestyle modifications, including weight loss, sodium restriction, increased physical activity and limited alcohol consumption. The PREMIER study was designed to assess the effects of 6 months of lifestyle modification or lifestyle modification plus the DASH diet on BP. The trial found that, compared with an advice-only control group, both intervention groups achieved clinically significant reductions in BP. However, compared with the lifestyle-only group, the addition on the DASH diet resulted in a small and nonsignificant decrease in BP (<1mm Hg), which could be accounted for by differ-

ential weight loss between the groups. The absence of a DASH diet only condition and greater weight loss in the lifestyle plus DASH treatment condition in PREMIER still make it impossible to determine the potential incremental benefit of the DASH diet in a 'free-living' setting.

5. Effects of Weight Loss on Blood Pressure

5.1 Obesity and Blood Pressure

The association between obesity and BP is well established, both cross-sectionally and longitudinally.[48] Although numerous interventional studies have examined the effect of weight loss on BP in overweight individuals, few have included hypertensive patients. Moreover, not all studies were designed to compare weight loss alone to a usual diet/exercise control condition, making it difficult to clarify the specific effect of weight loss on BP. Instead, some interventions: target multiple dietary components and/or multiple lifestyle components;[49] compare weight loss to another intervention, such as exercise;[50] include a dietary intervention for all groups;[51] or allow for changes in anti-hypertensive medication use. For example, Langford et al.[52] examined the DBP response of nine combinations of drugs and diets, including a placebo/weight-loss group and a placebo/usual diet group. However, 20% of placebo/usual diet participants were on step-up or open-label medication therapy by the end of the study. Thus, although the weight-loss group exhibited a BP reduction of 11.5/8.8mm Hg, this was not significantly different than the control group, which also displayed a decrease in BP. Moreover, results of such studies have shown significant reductions in BP resulting from weight loss (see Mulrow et al.[53] and Staessen et al.[54]).

In terms of magnitude of change, MacMahon et al.,[55] pooling results from a number of interventional studies, estimated that a weight loss of 9.2kg is associated with a reduction of 6.3mm Hg SBP and 3.1mm Hg DBP. More recent trials support these estimates, with clinically meaningful reductions of 7–10mm Hg SBP and 6–7mm Hg DBP following weight loss of approximately 8kg.[5,56] Thus, not only has the association between bodyweight and BP been well documented, interventional research strongly supports the efficacy of weight loss in reducing BP in both normotensive and hypertensive individuals who are overweight.

5.2 Exercise as a Means of Weight Loss

Although exercise is an important component of many weight management programmes, exercise alone is generally not associated with significant weight loss when diet is not modified. Most studies report decreases of <2kg bodyweight and <1–2% body fat in subjects who exercised from 6 weeks to 2 years.[57,58] Moreover, exercise is associated with minimal changes in hip-to-waist circumference ratio, suggesting also that body fat distribution is not greatly altered.[59] However, exercise appears to be associated with increased maintenance of weight loss,[60-62] which is important if BP changes associated with weight loss are to be sustained. In addition, there is evidence that exercise and diet may act synergistically to reduce bodyweight and improve aerobic capacity.[63] Interventions to promote weight loss often include an exercise component and supervised exercise enhances adherence as well as weight loss compared with simple instruction to increase exercise on one's own.[60] Presently, a behavioural weight loss programme that includes supervised exercise appears to be the most effective intervention to promote weight loss. In hypertensive patients, a combined exercise and weight-loss intervention has been shown to decrease SBP by 7.4–12.5mm Hg and DBP by 5.6–7.9mm Hg, respectively.[50,56]

6. Cardiac and Vascular Benefits of Behavioural Interventions

6.1 Left Ventricular Hypertrophy

Recently, there has been increased recognition of the significance of high BP as a marker of underlying vascular disease. An important consequence of high BP and the associated changes in the arterial vasculature is the development of LVH. Obesity is also associated with increased LV mass, causing increases in both wall thickness and chamber dimensions at all levels of BP.[64-66] In the general population and in cohorts with hypertension or IHD, increased LV mass is a predictor of cardiovascular

events independent of BP or other traditional risk factors.[9,10,67,68] One of the potential benefits of lowering BP is improved LV function and structure. Data from Framingham showed that regression of LVH was associated with a 25% reduction in cardiovascular mortality.[11] A number of studies have shown that regression of LVH may occur after BP is reduced with anti-hypertensive agents.[69-74] Although lifestyle studies have yielded conflicting results, data from Kokkinos et al.[75] and Hinderliter et al.[76] suggest that aerobic exercise training results in a decrease in LV mass. Similarly, several weight-reduction intervention trials have found that weight loss leads to a decrease in LV wall thickness.[77,78]

6.2 Arterial Stiffness

Early treatment trials focused on lowering DBP in order to reduce the risk of cardiovascular events. Evidence over the last 10 years has increasingly underscored the relatively greater importance of SBP,[79] and in the past 5 years pulse pressure also has emerged as a strong predictor of cardiovascular events and mortality.[80] The most important factor contributing to high SBP and elevated pulse pressure is arterial stiffness.[81,82] Although arterial stiffness and its clinical manifestations are most conspicuous in the elderly,[81] a recent large-scale study found that obesity was associated with increased pulse pressure,[83] and in patients with hypertension, obesity is related to reduced arterial distensibility.[84] Insulin resistance accompanying obesity is a likely pathophysiological mechanism, since reduced arterial distensibility is characteristic of insulin-dependent diabetes,[85,86] and in obese individuals, insulin's normally favourable effect on arterial stiffness is severely blunted.[87] Concentric LVH among hypertension patients also has been linked to reduced arterial distensibility.[88,89] Elevated pulse pressure may increase risk of myocardial ischaemia and related cardiac events because elevated SBP is associated with greater LV workload, whereas a decreased DBP may decrease coronary perfusion pressure.[90]

Aerobic fitness has been associated with reduced arterial stiffness in several cross-sectional studies.[91,92] However, in the Atherosclerosis Risk in Communities study, self-reported physical activity showed only a weak and inconsistent relationship to reduced arterial stiffness.[93] The latter findings may reflect limitations in self-report measures of physical activity. We are aware of only three studies to date that have reported the effects of exercise interventions on arterial stiffness, two of which observed an improvement. Tanaka at al.[94] studied 20 healthy middle-aged men who engaged in a 3-month aerobic exercise intervention and found arterial stiffness, assessed by carotid artery compliance using ultrasound imaging, to improve by 25%. Exercise training in heart failure patients also has been found to reduce arterial stiffness measured in the carotid artery.[95] However, a third study in 20 elderly patients with isolated systolic hypertension failed to show improved arterial stiffness after 8 weeks of moderate aerobic training; this null finding was interpreted as being a result of too short an intervention, and increased resistance to reversal of arterial stiffening in the elderly.[96]

6.3 Endothelial Function

An important vascular regulatory system that controls systemic vascular resistance (SVR) is the endothelial system. Several studies have shown endothelial dysfunction to be a characteristic of hypertension.[97-99] Impairment of flow-mediated dilation (FMD) of the brachial artery, an index of endothelial dysfunction, is associated with poor prognosis in hypertensive patients,[100] and is related to LVH in those with hypertension who have never received treatment for high BP.[101,102] High BP and elevated SVR secondary to endothelial dysfunction are thought to favour the development of concentric LVH.[103,104]

Both diet and exercise have been shown to influence endothelial function. A high-fat meal was found to result in attenuated FMD for several hours following its consumption.[105] A study evaluating the effects of a high-fat diet for 30 days observed that impaired FMD was evident even following overnight fasting.[106] In the latter study, a diet rich in fruit and vegetables for 30 days resulted in significantly greater FMD compared with the high-fat diet.[106] Aerobic exercise has been shown recently to result in improved FMD, in healthy middle-aged men and women,[107] and in patients with cardiovascular disease.[108,109] In hypertensive patients, the BP lowering effects of aerobic exercise has been

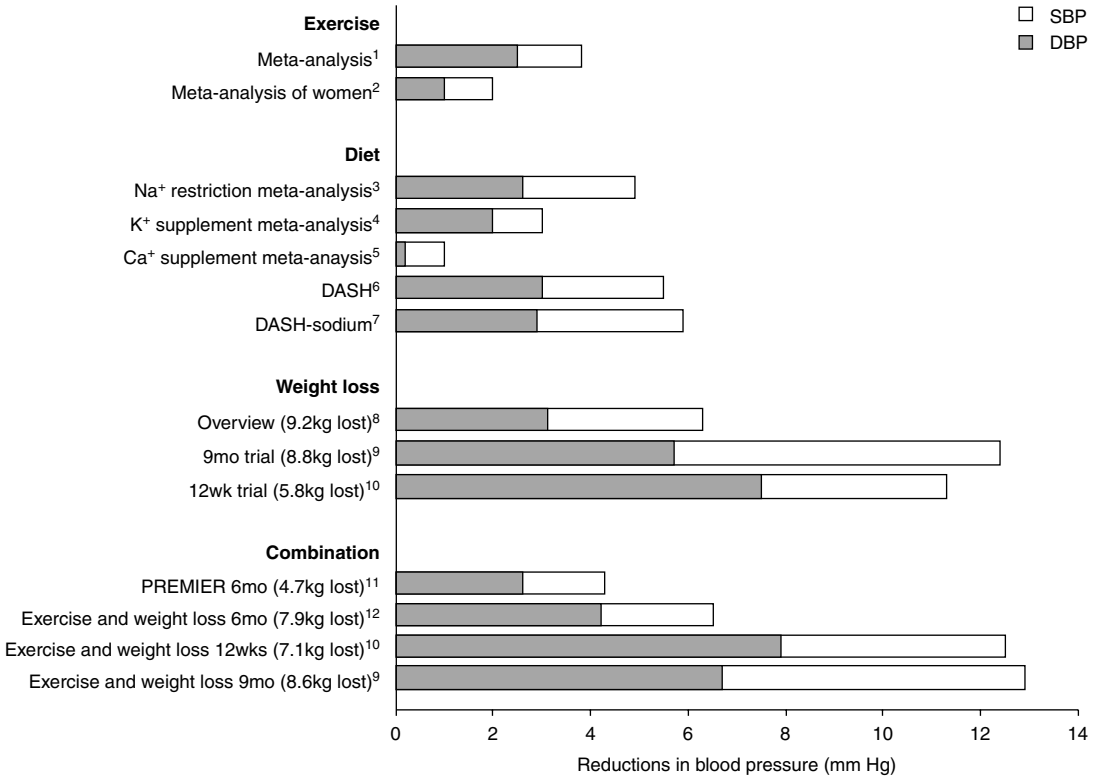

Fig. 1. Changes in clinic blood pressure in response to exercise, dietary, weight loss and combined lifestyle (exercise, diet and weight reduction) interventions in select studies. Results suggest that dietary changes and weight loss add to the benefits of exercise alone. 1 = Whelton et al.;[25] 2 = Kelley;[16] 3 = Cutler et al.;[31] 4 = Whelton et al.;[35] 5 = Allender et al.;[37] 6 = Appel et al.;[40] 7 = Sacks et al.;[43] 8 = MacMahon et al.;[55] 9 = Dengel et al.;[5] 10 = Gordon et al.;[50] 11 = Writing Group of the PREMIER Collaborative Research Group;[47] 12 = Blumenthal et al.[56] **DASH** = Dietary Approaches to Stop Hypertension; **DBP** = diastolic blood pressure; **SBP** = systolic blood pressure; * indicates study did not have a control group.

related to an improvement in endothelial function.[110] The mechanisms by which exercise may benefit endothelial function have yet to be fully elucidated, but may include increased bioavailability of nitric oxide[110,111] and suppression of postprandial lipidaemia.[112]

7. Conclusion

Although pharmacological treatment of high BP is effective in a large proportion of patients, drug therapy may be inconvenient and expensive, and may be associated with adverse effects. Behavioural interventions, such as exercise, diet (including lower alcohol consumption, reduced sodium intake, adequate potassium intake, increasing the quantity of fruits, vegetables, nuts, and low-fat diary products consumed, and decreasing the amount of saturated fat eaten), and weight loss, may complement or provide an alternative to anti-hypertensive medications. These behavioural interventions have been shown to reduce SBP and DBP (see figure 1). For obese patients, a combined exercise/weight-loss therapy has been seen to be more effective than treatment with exercise or weight loss on their own. The influence of these behavioural interventions on BP might be mediated by beneficial adaptations in the cardiovascular system with regression of LVH, decreased arterial stiffness, and improved endothelial function. These data support the role of behavioural interventions in the treatment of patients with elevations in BP.

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