

COMMENTARY

Uncontrolled hypertension: beyond pharmacological treatment

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Hypertension remains the leading cause of mortality and the third largest cause of disability in both developed and developing countries. Worldwide, in 2001, 7.6 million premature deaths, 54% of stroke cases and 47% of ischemic heart disease cases were attributed to high blood pressure (BP).¹ The number of adults with hypertension in 2025 was predicted to be as many as 1.5 billion people worldwide.²

Despite the development of new antihypertensive medications and a better understanding of the physiology of high BP, control rates remain low. Data available from the National Health and Nutrition Examination Survey 2003–2004 show that two out of three patients with hypertension had uncontrolled BP, and control rates decreased according to age.³ In the same study, control rates were 71.7, 63.5 and 50.0% among treated hypertensive patients aged 18–39, 40–59 and ≥60 years, respectively. Factors that predispose individuals to uncontrolled hypertension include advanced age, obesity, high dietary salt intake, poor adherence to antihypertensive treatment, decreased physical activity, use of agents (for example, nonsteroidal anti-inflammatory drugs) that increase BP and the presence of secondary endocrine causes.⁴ Moreover, increased attention to systolic BP elevation and newer stricter treatment goals set by guideline committees have made it more difficult for physicians to attain ‘control’ as it is currently defined.⁴

In this issue of *Hypertension Research*, Carlsson *et al.*⁵ analyzed the cardiovascular

risk factor profiles of 60-year-old patients with previously diagnosed hypertension and evaluated the lifestyle and socioeconomic factors associated with uncontrolled hypertension in this population. Dyslipidemia and metabolic syndrome were highly prevalent among patients with hypertension. In addition, waist circumference and avoidance of health care for financial reasons were positively associated with uncontrolled hypertension, whereas coronary heart disease and daily fruit intake were negatively associated with uncontrolled BP in men. Among women, waist circumference was positively associated with uncontrolled BP, whereas the presence of coronary heart disease and living in an apartment both had negative associations.

The presence of multiple cardiovascular risk factors in the particular Swedish population studied by Carlsson *et al.* deserves special attention. More than 40% of patients with hypertension had metabolic syndrome, and a majority of them had high or medium–high cardiovascular risk on the basis of their apolipoprotein ratio. According to the Framingham Heart study, hypertension occurs in isolation as a cardiovascular risk factor in <20% of hypertensive patients.⁶ Risk factor clustering greatly increases the risk of cardiovascular disease. Approximately 63% of coronary heart disease in the Framingham population occurred in men with two or more additional risk factors.⁶

As pointed out by the authors, this study is limited by its cross-sectional design, which prevents definitive conclusions regarding cause and effect among the relationships discussed. Nevertheless, the study by Carlsson *et al.* strengthens the concept that uncontrolled hypertension is a multifactorial entity related not only to medical factors but also to social, economic and nutritional issues.

Clinical inertia, defined as a provider’s reluctance to increase therapy when treatment goal is not reached, may partially explain the findings of Carlsson *et al.* Only 80% of men and 78% of women with uncontrolled hypertension were taking antihypertensive agents. Furthermore, 50% of men and 51% of women with uncontrolled BP were taking a single agent. The reasons for an apparently inadequate treatment in these patients were not explored in this study; thus, the degree to which clinical inertia contributed cannot be determined.

Other factors that may have had a greater or lesser role include the white coat effect and secondary forms of hypertension. As information regarding the clinical setting in which physical examinations were carried out (and by whom) was not provided, the extent to which the white coat effect may have affected BP levels and led to an overestimation of the prevalence of uncontrolled hypertension in this study cannot be ascertained. The search for secondary forms of hypertension brings with it the opportunity to not only improve hypertension control but also cure it altogether. In particular, primary aldosteronism is now recognized as a common, specifically treatable and potentially curable cause of hypertension affecting 5–10% of patients within the general hypertensive population.⁷ Among patients with resistant hypertension (defined as hypertension uncontrolled despite three or more antihypertensive medications), the prevalence is even higher.⁴ It is possible that, had primary aldosteronism been actively sought in the study by Carlsson *et al.*, it might have been found to account for a significant proportion of their hypertensive patients, and especially among those whose hypertension was uncontrolled.

Achieving optimal BP control is the most important single issue in the management of

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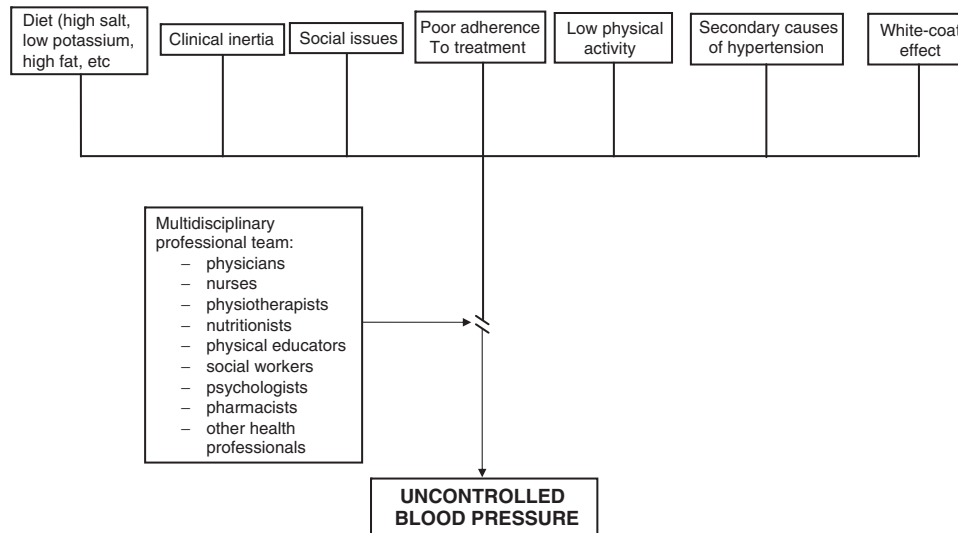


Figure 1 Factors related to uncontrolled blood pressure and the importance of a multidisciplinary professional approach.

hypertension; in most hypertensive patients, it is difficult or impossible to control BP using one drug. For example, in the ALLHAT (Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack) trial, <30% of more than 42 000 participants achieved target BP (<140/90 mm Hg) on monotherapy.⁸ In the LIFE (Losartan Intervention For Endpoint) trial, in which treatment to goal (<140/90 mm Hg) was aggressively pursued in >9000 patients with left ventricular hypertrophy and an average baseline BP of 175/98 mm Hg, >90% required more than one antihypertensive agent.⁹

Recognition of the factors related to uncontrolled hypertension provides data for health-care agencies to create strategies to improve BP control and reduce cardiovascular risk. The relationship between uncontrolled BP and multiple factors highlights the importance of a multiple professional approach to the treatment of patients with hypertension (Figure 1). The involvement of nurses, physiotherapists, nutritionists, physical educators, social workers, psychologists, pharmacists and other health professionals in the care of hypertensive patients can increase BP control rates. For example, in the DREAM 3 (Diabetes Risk Evaluation and Microalbuminuria) study, two community-based strategies for controlling hypertension were compared.¹⁰ In the intervention group, a home-care nurse followed a predefined treatment algorithm of pharmacological antihypertensive therapy. In the control group, treatment decisions were made by each individual's primary care physician. After 12

months of follow-up, the group randomized to having the nurse implement a treatment strategy for BP control had better results in lowering diastolic rather than systolic BP compared with home care visits for BP monitoring alone and follow-up treatment by a family physician.

Obesity is a common finding in patients with uncontrolled hypertension, for which a multiple professional approach is required. In the study by Carlsson *et al.*, waist circumference was independently associated with uncontrolled hypertension in both men and women. Weight loss is more likely to be achieved when a team of multidisciplinary health professionals, such as nutritionists, psychologists and physical educators, is involved in the care of obese patients.

Nutritionists are especially important for hypertensive patients for providing not only a low-calorie diet but also a low-salt diet. Although dietary salt was not explored in the study by Carlsson *et al.*, there is a strong relationship between dietary salt and severity of hypertension. For example, in the Dietary Approaches to Stop Hypertension (DASH) trial, 412 patients with mild–moderate hypertension (range: 120–159/80–95 mm Hg) were randomized to the DASH diet (which is rich in vegetables, fruits and low-fat dairy products) or to a control diet.¹¹ Each group received increasing levels of dietary sodium (50, 100, 150 mmol per 24 h) for 30 consecutive days in a cross-over design. Compared with the control diet with a high dietary sodium intake, the DASH diet and low dietary sodium intake lowered systolic BP by 11.5 mm Hg in participants with hyperten-

sion (12.6 mm Hg for blacks; 9.5 mm Hg for others).

In conclusion, uncontrolled hypertension is common in clinical practice and is a multifactorial condition, not just a reflection of inadequate prescribing of medication. The recognition that uncontrolled hypertension can be related to various factors, which should be evaluated, and that the involvement of a multidisciplinary professional team facilitates education and motivation toward improved medication compliance and healthier lifestyles offers means by which control of hypertension may be achieved more often, thereby reducing the impact and cost of associated cardiovascular disease.

- 1 Lawes CM, Vander Hoorn S, Rodgers A, International Society of Hypertension. Global burden of blood-pressure-related disease, 2001. *Lancet* 2008; **371**: 1513–1518.
- 2 Kearney PM, Whelton M, Reynolds K, Muntner P, He J. Global burden of hypertension: analysis of worldwide data. *Lancet* 2005; **365**: 217–223.
- 3 Ong KL, Cheung BM, Man YB, Lau CP, Lam KS. Prevalence, awareness, treatment and control of hypertension among United States adults 1999–2004. *Hypertension* 2007; **49**: 69–75.
- 4 Pimenta E, Gaddam KK, Oparil S. Mechanisms and treatment of resistant hypertension. *J Clin Hypertens* 2008; **10**: 239–244.
- 5 Carlsson A, Wändell PE, Jourmath G, de Faire U, Hellénus ML. Factors associated with uncontrolled hypertension and cardiovascular risk in hypertensive 60-year-old men and women—a population-based study. *Hypertens Res* 2009; **32**: 780–785.
- 6 Kannel WB. Blood pressure as a cardiovascular risk factor: prevention and treatment. *JAMA* 1996; **275**: 1571–1576.
- 7 Mulatero P, Stowasser M, Loh KC, Fardella CE, Gordon RD, Mosso L, Gomez-Sanchez CE, Veglio F, Young Jr

- WF. Increased diagnosis of primary aldosteronism, including surgically correctable forms, in centers from five continents. *J Clin Endocrinol Metab* 2004; **89**: 1045–1050.
- 8 Cushman WC, Ford CE, Cutler JA, Margolis KL, Davis BR, Grimm RH, Black HR, Hamilton BP, Holland J, Nwachuku C, Papademetriou V, Probstfield J, Wright Jr JT, Alderman MH, Weiss RJ, Piller L, Bettencourt J, Walsh SM, ALLHAT Collaborative Research Group. Success and predictors of blood pressure control in diverse North American settings: the Antihypertensive Lipid-Lowering treatment to prevent Heart Attack Trial (ALLHAT). *J Clin Hypertens* 2002; **4**: 393–404.
- 9 Dahlöf B, Devereux RB, Kjeldsen SE, Julius S, Beevers G, de Faire U, Fyhrquist F, Ibsen H, Kristiansson K, Lederballe-Pedersen O, Lindholm LH, Nieminen MS, Omvik P, Oparil S, Wedel H, LIFE Study Group. CV morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomized trial against atenolol. *Lancet* 2002; **359**: 995–1003.
- 10 Tobe SW, Pylypchuk G, Wentworth J, Kiss A, Szalai JP, Perkins N, Hartman S, Ironstand L, Hoppe J. Effect of nurse-directed hypertension treatment among First Nations people with existing hypertension and diabetes mellitus: the Diabetes Risk Evaluation and Microalbuminuria (DREAM 3) randomized controlled trial. *CMAJ* 2006; **174**: 1267–1271.
- 11 Sacks FM, Svetkey LP, Vollmer WM, Appel LJ, Bray GA, Harsha D, Obarzanek E, Conlin PR, Miller III ER, Simons-Morton DG, Karanja N, Lin PH, DASH-Sodium Collaborative Research Group. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. *N Engl J Med* 2001; **344**: 3–10.