Editorial Comment

Focus on Masked Workplace Hypertension: The Next Step for Perfect 24-Hour Blood Pressure Control

Hideyuki UNO[1] and Kazuomi KARIO[2]

(*Hypertens Res* 2006; 29: 937–940)

***Key Words*: masked workplace hypertension, job strain, metabolic syndrome, gene**

The relationship between occupation and adverse health effects has been studied throughout the world. In the past, most of these studies focused on the direct examination of physical adverse effects. More recently, there has been a growing interest in the examination of mental adverse effects, due to the emergence of social problems such as suicide and *karoshi* (literally, "death from overwork") (*1*) caused by chronic stress at work, and because the proportion of white-collar workers has increased. Many studies on the relationship between occupation and blood pressure or cardiovascular diseases have been performed since the 1970s. This relationship has been evaluated in various kinds of workers: white-collar workers (*2*), pilots (*3*), transit operators (*4*), and so on.

Masked hypertension, in which blood pressure increases in daily life in spite of normotension in a clinic, has also been a subject of increasing interest (*5*). There are three kinds of masked hypertension: morning hypertension, nocturnal hypertension and stress hypertension (Fig. 1) (*6*, *7*). From the beginning, it has long been estimated that approximately 10% of hypertensives have higher blood pressure at home than in the clinic (*8*, *9*). In addition, job strain, defined as high psychological demands plus low decision latitude at work, causes increase of blood pressure (*10*). Job strain is a risk factor for hypertension, particularly in hard working men (*11*). Some people have been reported to have higher blood pressures at work than in the clinic (*12*). Therefore, masked stress-induced hypertension at work is a subject of increasing interest.

Job strain causes an increase in ambulatory blood pressure at work, at home, and during sleep (*13*). A previous study reported that ambulatory blood pressures were higher than clinic blood pressures in normotensive subjects, whereas the reverse was typically true in hypertensives (*14*). In other words, individuals who are clinically normotensive may still experience higher ambulatory blood pressure at work. Masked stress-induced hypertension may develop into sustained hypertension (high blood pressure daily life) as a result of chronic stress due to job strain. In addition, of course, other factors also play a role in blood pressure increase, including smoking (*9*, *13*, *15–17*) and alcohol (*13*, *15*). Masked hypertensives and sustained hypertensives are at equivalent risk for developing cardiovascular diseases (*15*, *18*, *19*). Risk factors of left ventricular mass index increases in masked hypertensives caused by job strain (*10*). Masked stress-induced hypertension may lead to target organ damage in workers (*20–28*).

From a mechanistic point of view, masked stress-induced hypertension may result from an increase in vascular tone caused by sympathetic vasoconstrictor activity (*29*) and a high level of cortizol in peripheral blood (*30*). Surge in morning blood pressure (Monday morning surge) (*31*) and the rate of cardiovascular sudden deaths (*32*) are said to be higher on Monday than on the other days of the week. This may be because workers experience pronounced strain and stress on Monday due to the relative absence of these sensations over the weekend, just as the rate of angina pectoris attacks in dynamite factory workers is well known to be highest on

From the [1]Division of Community and Family Medicine, Center for Community Medicine and [2]Division of Cardiovascular Medicine, Jichi Medical University School of Medicine, Shimotsuke, Japan.

Address for Reprints: Kazuomi Kario, M.D., COE (Center of Excellence) Program, Division of Cardiovascular Medicine, Jichi Medical University School of Medicine, 3311–1, Yakushiji, Shimotsuke 329–0498, Japan. E-mail: kkario@jichi.ac.jp

Received October 24, 2006.

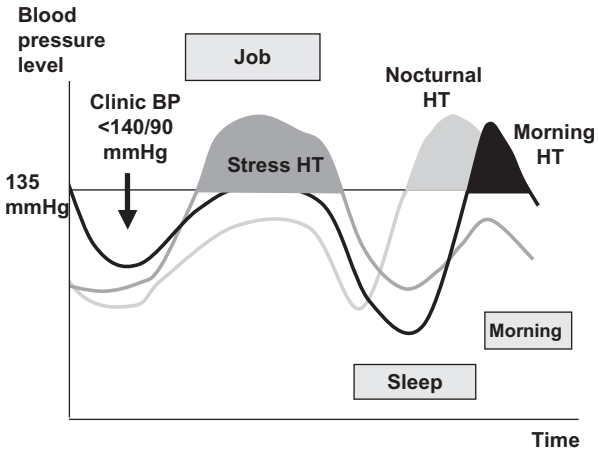

Fig. 1. *Three kinds of masked hypertension: morning hypertension, nocturnal hypertension and stress hypertension.*

Monday (Monday morning attack) due to the reduced exposure to nitro compounds.

On the other hand, the relationship between metabolic syndrome and blood pressure has also been a focus of research around the world. We think that masked hypertension at work, as at home (*8*), may be related with overweight, high insulin levels and low high-density lipoprotein (HDL) cholesterol. As industrial physicians, we have observed that the rate of overweight and obesity in workers has increased in recent years. It has been reported that obesity leads to metabolic syndrome, and that two-thirds of subjects with high-normal blood pressure who did not receive treatment for 4 years or more developed hypertension (*33*). Normotensives with metabolic syndrome may develop true sustained hypertension. Hypertension is said to be the most common component of metabolic syndrome (*34*). We think it more accurate to regard normotensives with metabolic syndrome as potential prehypertensives. Therefore, for the industrial physician the most important question is how to identify workers with masked hypertension and target organ damage, so that they can take preventive measures. As the measures, we think that setting up a cut-off value of blood pressure would be useful for the prevention of metabolic syndrome (*35*) or along with the early detection of useful risk factors. Harada *et al*. reported that the most adequate cut-off value of blood pressure at annual examination may be 130/85 mmHg for predicting 140/90 mmHg at work (*36*), and that useful risk factors may be a family history of hypertension, body mass index and age (*36*). This report (*36*) is particularly noteworthy from the standpoint of the study of masked stress-induced hypertension at work. Unfortunately, however, these authors did not describe the relationship between masked hypertension at work and job strain. Nonetheless, this relationship—the association between blood pressure and work—will continue to become more and more important.

Family history of hypertension was a useful risk factor for the early identification of masked hypertension at work (*36*). The analyses into various polymorphisms of hormones and diseases develop, and the relationship between adrenergic receptor polymorphisms and blood pressure was studied (*37–42*). These reports (*37–41*) described that the effects of various adrenergic receptor polymorphisms on agonist-mediated vascular desensitization were different. The remaining study (*42*) examined the relationship between mental stress and adrenergic receptor genotypes, and described that increase of blood pressure depended on these genotypes. Masked stress-induced hypertension may have an influence on adrenergic receptor genotypes. It has been reported that renin-angiotensin system genotypes are related to premature hypertension (*43*). If some of these genotypes, which may have a major influence on the pharmacodynamic determinants of antihypertensive response, could be identified, this could tie in the early findings and treatment of masked stress-induced hypertension at work. However, an emerging consensus is that single genes have only small effects on antihypertensive drug responses, and even the combined effects of all presently known polymorphisms do not account for enough variation in response to be clinically useful (*44*). Additional studies, including studies considering the effects of haplotypes and multilocus genotypes on drug response, gene-by-environment interactions and new genome-wide scanning techniques that may lead to the identification of genes previously unsuspected of influencing drug response, are underway.

Refereces

1. Yoshimura T: Occupational health. *J Epidemiol* 1996; **6**: s115–s120.
2. Guimont C, Brisson C, Dagenais GR, *et al*: Effects of job strain on blood pressure: a prospective study of male and female white-collar workers. *Am J Public Health* 2006; **96**: 1436–1443.
3. Tomei F, De Sio S, Tomao E, *et al*: Occupational exposure to noise and hypertension in pilots. *Inter J Environ Health Res* 2005; **15**: 99–106.
4. Greiner BA, Krause N, Tragland D, Fisher JM: Occupational stressors and hypertension: a multi-method study using observer-based job analysis and self-reports in urban transit operators. *Soc Sci Med* 2004; **59**: 108–194.
5. Pickering TG, Davidson K, Gerin W, Schwartz JE: Masked hypertension. *Hypertension* 2002; **40**: 795–796.
6. Kario K, Ishikawa J, Pickering TG, *et al*: Morning hypertension: The strongest independent risk factor for stroke in elderly hypertensive patients. *Hypertens Res* 2006; **29**: 581–587.
7. Kario K: Clinician's Manual on Early Morning Risk Management in Hypertension. London, Science Press, 2004, pp 1–68.
8. Shahab ST, Gudbrandsson T, Jamerson K, Julius S: Isolated "home hypertension" in Tecumseh, Michigan. *Croat Med J* 1993; **34**: 325–331.
9. Bobrie G, Genes N, Vaur L, *et al*: Is "isolated home" hyper-

tension as opposed to "isolated office" hypertension a sign of greater cardiovascular risk? *Arch Intern Med* 2001; **161**: 2205–2211.
10. Schnall PL, Pieper C, Schwartz JE, *et al*: The relationship between 'job strain,' workplace diastolic blood pressure, and left ventricular mass index. Results of a case-control study. *JAMA* 1990; **263**: 1929–1935.
11. Light KC, Turner JR, Hinderliter AL: Job strain and ambulatory work blood pressure in healthy young men and women. *Hypertension* 1992; **20**: 214–218.
12. Fiedler N, Favata E, Goldstein BD, Gochfeld M: Utility of occupational blood pressure screening for the detection of potential hypertension. *J Occup Med* 1988: **30**: 943–948.
13. Schnall PL, Schwartz JE, Landsbergis PA, Warren K, Pickering TG: Relation between job strain, alcoholic, and ambulatory blood pressure. *Hypertension* 1992; **19**: 488–494.
14. James GD, Pickering TG, Yee LS, Harshfield GA, Riva S, Laragh JH: The reproducibility of average ambulatory, home, and clinic pressures. *Hypertension* 1988; **11**: 545–549.
15. Bobrie G, Chatellier G, Genes N, *et al*: Cardiovascular prognosis of "masked hypertension" detected by blood pressure self-measurement in elderly treated hypertensive patients. *JAMA* 2004; **291**: 1342–1349.
16. Selenta C, Hogan BE, Linden W: How often do office blood pressure measurements fail to identify true hypertension? An exploration of white-coat normotension. *Arch Fam Med* 2000; **9**: 533–540.
17. Mann SJ, James GD, Wang RS, Pickering TG: Elevation of ambulatory systolic blood pressure in hypertensive smokers. A case-control study. *JAMA* 1991; **265**: 2226–2228.
18. Bjorklund K, Lind L, Zethelius B, Andren B, Lithell H: Isolated ambulatory hypertension predicts cardiovascular morbidity in elderly men. *Circulation* 2003; **107**: 1297–1302.
19. Clement DL, De Buyzere ML, De Bacquer DA, *et al*, Office *versus* Ambulatory Pressure Study Investigators: Prognostic value of ambulatory blood-pressure recordings in patients with treated hypertension. *N Engl J Med* 2003; **348**: 2407–2415.
20. Mancia G, Parati G: Ambulatory blood pressure monitoring and organ damage. *Hypertension* 2000; **36**: 894–900.
21. Devereux RB, Pickering TG: Relationship between the level, pattern and variability of ambulatory blood pressure and target organ damage in hypertension. *J Hypertens* 1991; **8**: s34–s38.
22. Parati G, Pomidossi G, Albini F, Malaspina D, Mancia G: Relationship of 24-hour blood pressure mean and variability to severity of target organ damage. *J Hypertens* 1987; **5**: 93–98.
23. Liu JE, Roman MJ, Pini R, Schwartz JE, Pickering TG, Devereux RB: Cardiac and arterial target organ damage in adults with elevated ambulatory and normal office blood pressure. *Ann Intern Med* 1999; **131**: 564–572.
24. Mancia G, Zanchetti A, Agabiti-Rosei E, *et al*: Ambulatory blood pressure is superior to clinic blood pressure in predicting treatment-induced regression of left ventricular hypertrophy. *Circulation* 1997; **95**: 1464–1470.
25. Fagard RH, Staessen JA, Thijs L: Relationship between-changes in left ventricular mass and in clinic and ambulatory blood pressure in response to antihypertensive therapy. *J Hypertens* 1997; **15**: 1493–1502.
26. Redon J, Campos C, Narciso ML, Rodicio JL, Pascual JM, Ruilope LM: Prognostic value of ambulatory blood pressure monitoring in refractory hypertension. *Hypertension* 1998; **31**: 712–718.
27. Fagard R, Staessen JA, Thijs L: Prediction of cardiac structure and function by repeated clinic and ambulatory blood pressure. *Hypertension* 1997; **29**: 22–29.
28. Eguchi K, Kario K, Shimada K: Greater impact of coexistence of hypertension and diabetes on silent cerebral infarcts. *Stroke* 2003; **34**: 2471–2474.
29. Panza JA, Epstein SE, Quyyumi AA: Circadian variation in vascular tone and its relation to alpha-sympathetic vasoconstrictor activity. *N Engl J Med* 1991; **325**: 986–990.
30. Steptoe A, Siegrist J, Kirschbaum C, Marmot M: Effort-reward imbalance, overcommitment, and measures of cortizol and blood pressure over the working day. *Psychosom Med* 2004; **66**: 323–329.
31. Murakami S, Otsuka K, Kubo Y, *et al*: Repeated ambulatory monitoring reveals a Monday morning surge in blood pressure in a community-dwelling population. *Am J Hypertens* 2004; **17**: 1179–1183.
32. Arntz HR, Willich SN, Schreiber C, Bruggemann T, Stern R, Schultheiss HR: Diurnal, weekly and seasonal variation of sudden death. Population-based analysis of 24, 061 consecutive cases. *Eur Heart J* 2000; **21**: 315–320.
33. Julius S, Nesbitt SD, Egan BM, *et al*, Trial of Preventing Hypertension (TROPHY) Study Investigations: Feasibility of treating prehypertension with an angiotensin-receptor blocker. *N Engl J Med* 2006; **354**: 1685–1697.
34. Ishizaki N, Ishizaki Y, Toda E, Hashimoto H, Nagai R, Yamakado M: Hypertension is the most common component of metabolic syndrome and the greater contributor to carotid arteosclerosis in apparently healthy Japanese individuals. *Hypertens Res* 2005; **28**: 27–34.
35. Takeuchi H, Saitoh S, Takagi S, *et al*: Meatabolic syndrome and cardiac disease in Japanese men: applicability of the concept of metabolic syndrome defined by the National Cholesterol Education Program–Adult Tyreatment Panel III to Japanese men—the Tanno and Sobetsu Study. *Hypertens Res* 2005; **28**: 203–208.
36. Harada K, Karube Y, Saruhara H, Takeda K, Kuwajima I: Workplace hypertension is associated with obesity and family history. *Hypertens Res* 2006; **29**: 969–976.
37. Yuan M, Ohishi M, Ito N, *et al*: Genetic influences of β adrenoceptor polymorphisms on arterial functional changes and cardiac remodeling in hypertensive patients. *Hypertens Res* 2006; **29**: 875–881.
38. Jie Liu, Zhao-Qian Liu, Bang-Ning Yu, *et al*: β1-Adrenergic receptor polymorphisms influence the response to metoprolol monotherapy in patients with essential hypertension. *Clin Pharmacol Ther* 2006; **77**: 23–32.
39. Sofowora GG, Dishy V, Landau R, *et al*: Alpha1A-adrenergic receptor polymorphism and vascular response. *Clin Pharmacol Ther* 2004; **75**: 539–545.
40. Sofowora GG, Dishy V, Muszkat M, *et al*: A common beta1-adrenergic receptor polymorphism (Arg389Gly) affects blood pressure response to beta-blockade. *Clin Pharmacol Ther* 2003; **74**: 366–371.
41. Dishy V, Sofowora GG, Xie HG, *et al*: The effect of com-

mon polymorphisms of the β2-adrenergic receptor on agonist-mediated vascular desensitization. *N Engl J Med* 2001; **345**: 1030–1035.
42. McCaffery JM, Pogue-Geile MF, Ferrell RE, Petro N, Manuck SB: Variability within alpha- and beta-adrenoreceptor genes as a predictor of cardiovascular function at rest and in response to mental challenge. *J Hypertens* 2002; **20**: 1105–1114.
43. Barbalic M, Skaric-Juric T, Cambien F, *et al*: Gene polymorphisms of the rennin-angiotensin system and early development of hypertension. *Am J Hypertens* 2006; **19**: 837–842.
44. Schwartz GL, Turner ST: Pharmacogenetics of antihypertensive drug responses. *Am J Pharmacogenomics* 2004; **4**: 151–160.