Caution for Winter Morning Surge in Blood Pressure

A Possible Link With Cardiovascular Risk in the Elderly

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There are variations in the onset of cardiovascular events. As diurnal variation, most studies have shown an increased incidence of acute cardiovascular events such as acute myocardial infarction, sudden cardiac death, and stroke in the morning.[1] In addition, weekly and seasonal variations in the cardiovascular events have also been reported.[2] These variations may be closely associated with ambulatory blood pressure (BP) variations. In this issue, Modesti et al report an interesting study demonstrating weather-related change in ambulatory BP profile.[3] In their study, in addition to poorly controlled nighttime BP in hot days, cold weather was significantly associated with increased morning BP surge in elderly subjects, even when they were treated with a higher number of antihypertensive drugs per day in cold weather. This cold weather–augmented morning BP surge may partly account for an increased number of cardiovascular events in the cold morning during the winter season.

Ambulatory BP also exhibits significant diurnal variation, and an abrupt BP surge in the morning has been suggested as a possible trigger for cardiovascular events. Previously, there were several areas of evidence indicating the importance of morning BP surge on cardiovascular disease. There are 2 relatively small prospective studies to support the possible risk of morning BP surge and cardiovascular events. The first is the Jichi Medical School (JMS) ambulatory blood pressure monitoring (ABPM) study (Wave 1) on elderly hypertensive patients[4]; the other is a French study on hypertensive patients.[5] In the JMS ABPM, a prospective study of 519 elderly hypertensive patients with mean age of 72 years, brain MRI was conducted to assess silent cerebrovascular disease together with 24-hour ABPM at baseline. The prognosis for stroke was studied during the follow-up period of 41 months. Both the sleep–trough surge (morning BP level minus the lowest nocturnal BP) and waking surge (morning BP minus prewaking BP) were significantly associated with stroke risk independently of 24-hour BP levels and nocturnal BP dipping. A recent French prospective study of 507 patients with hypertension found similar results.[5] Hypertensive patients were divided into quartiles of waking surge, defined as morning systolic BP measured on standing minus systolic BP before rising. Although there were no significant differences in the 24-hour BP levels between each group, cardiovascular complications occurred more frequently during the follow-up period in the higher quartile groups. In the multivariate analysis, the waking morning BP surge was significantly associated with cardiovascular risk independent of age and 24-hour BP level.

Morning BP surge is also significantly associated with hypertensive target organ damage. In the JMS ABPM study (Wave 1), silent cerebral infarct was measured by brain MRI at baseline and was more frequently detected in the morning surge group than in the nonsurge group, particularly multiple silent cerebral infarcts.[4] Exaggerated morning BP surge also appeared to increase hypertensive heart disease. In our community-dwelling subjects, sleep-rough surge adjusted for morning physical activity was significantly correlated with left ventricular (LV) mass index, assessed by echocardiography,[6] as found in the French study.[5] Morning BP minus evening BP assessed self-measured BP, also independent determinants of LV mass in hypertensive patients.[7] In addition, hypertensive patients with morning BP surge had prolonged corrected QT interval (QTc) duration and QTc dispersion compared with those without morning BP surge.[8] These QTc abnormalities found in the morning BP surge groups were only significant in the morning period. Spectral analysis of heart rate variability showed that the low frequency power/high frequency power ratio, an indirect index of sympathetic activity, was significantly higher in the morning BP surge group than in the nonsurge group. Thus, in the surge groups, increased sympathetic activity in the morning leads to prolonged QTc dispersion. As this increased QTc dispersion is reported to be associated with LV hypertrophy and cardiac arrhythmia, exaggerated morning BP surge also appears to be associated with increased risk of cardiac arrhythmia and sudden death in the morning in hypertensive patients. More recently, untreated hypertensive patients with morning BP surge had increased carotid intima-medial thickness (IMT) and higher levels of inflammatory markers, such as interleukin (IL) 6 and C-reactive protein, than those without morning BP surge.[9] Another recent study also demonstrated that increased time rate of BP variation in the morning was independently associated with increased carotid IMT in untreated hypertensive patients.[10] These studies indicated that morning BP surge would be potential cardiovascular risk in hypertensive patients.

Increased sympathetic activity, particularly α-adrenergic component, increases vascular tone in the resistance arteries and may contribute to the morning BP surge. In fact, the bedtime dosing of α-adrenergic blocker reduced preferen-

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tially morning BP levels and morning BP surge than ambulatory BPs during another period, particularly in those with advanced hypertensive cerebrovascular disease.[11] As the cold stimulation is also known to have pressor effect predominantly through α-adrenergic activation, cold weather would augment morning BP surge synergically through α-adrenergic activation. Psychological stress also predominantly activates α-adrenergic activity, and the recent study using 7-day (24-hour) ambulatory BP monitoring demonstrated that morning BP surge was the greatest on Monday among days of the week in community-dwelling subjects.[12] This Monday morning surge in BP may be in accord with clinical evidence that cardiovascular events more frequently occur in the morning on Monday. Thus, variations in ambulatory BP would be parallel to the incidence of cardiovascular events. Various peaks of ambulatory BP may be additively or synergically associated with each other to increase the risk of cardiovascular disease. Further experimental and clinical studies are necessary to clarify the impact of these variations of cardiovascular risk on cardiovascular disease in hypertensive patients.

Thrombotic tendency such as endothelial cell dysfunction, platelet activation, and hypercoagulable and hypofibrinolytic states is potentiated in the morning. Fibrinogen, a well-established thrombotic risk factor, has seasonal variations with a winter peak in the elderly.[13] Thus, particularly in winter, in addition to conventional antihypertensive therapy, specific strategy targeting morning BP and its surge would practically achieve more effective prevention for cardiovascular events in the morning in elderly hypertensive patients.

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