Weather-related changes in 24-hour blood pressure profile: effects of age and implications for hypertension management.

Weather-Related Changes in 24-Hour Blood Pressure Profile

Effects of Age and Implications for Hypertension Management

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Abstract**—**A downward titration of antihypertensive drug regimens in summertime is often performed on the basis of seasonal variations of clinic blood pressure (BP). However, little is known about the actual interaction between outdoor air temperature and the effects of antihypertensive treatment on ambulatory BP. The combined effects of aging, treatment, and daily mean temperature on clinic and ambulatory BP were investigated in 6404 subjects referred to our units between October 1999 and December 2003. Office and mean 24-hour systolic BP, as well as morning pressure surge, were significantly lower in hot (>90th percentiles of air temperature; 136±19, 130±14, and 33.3±16.1 mm Hg; $P<0.05$ for all), and higher in cold (<10th percentiles) days (141±12, 133±11, and 37.3±9.5 mm Hg; at least $P<0.05$ for all) when compared with intermediate days (138±18, 132±14, and 35.3±15.4 mm Hg). At regression analysis, 24-hour and daytime systolic pressure were inversely related to temperature ($P<0.01$ for all). Conversely, nighttime systolic pressure was positively related to temperature ($P<0.02$), with hot days being associated with higher nighttime pressure. Air temperature was identified as an independent predictor of nighttime systolic pressure increase in the group of elderly treated hypertensive subjects only. No significant relationship was found between air temperature and heart rate. Our results show for the first time that hot weather is associated with an increase in systolic pressure at night in treated elderly hypertensive subjects. This may be because of a nocturnal BP escape from the effects of a lighter summertime drug regimen and may have important implications for seasonal modulation of antihypertensive treatment. (***Hypertension*****. 2006;47:155-161.)**

Key Words: blood pressure monitoring, ambulatory ■ hypertension ■ aging

Several studies have reported that blood pressure (BP) values obtained both in the clinic and in ambulatory conditions are lower in hot than in cold months, which is also the case in a general population.[1] In summer, a reduction in cardiovascular mortality has also been observed,[2,3] with a reduction in the occurrence of stroke in hypertensive patients.[4,5] These findings might support the practice of downward titration of antihypertensive drug regimens, especially in the elderly. However, this clinical practice is not embodied in any of the guidelines.[6,7] Moreover, there is limited information regarding the effects of changes in daily mean outdoor air temperature (Ta) on ambulatory BP (ABP) in the elderly, in particular, in aged hypertensive subjects. Finally, no information is available on whether a clinic BP-guided reduction in the dosage of antihypertensive drug, in the case of hot weather, might be responsible for a reduced coverage of BP over 24 hours. The need to clarify these issues is underlined by the observation that older hypertensive patients do not show the same reduction in morbidity and mortality during hot months as younger subjects do.[3]

The aim of the present study was, therefore, to more deeply investigate the climate-related changes in clinic and ABP and heart rate in subjects referred to our institutions for BP assessment during a 4-year period. This was done with special attention to the possible interaction between outdoor temperature–related BP changes, aging, and prescription of antihypertensive treatment.

Methods

Subjects

All of the outpatients referred to the Hypertension Clinics of the Clinica Medica of the University of Florence and of the Istituto Auxologico Italiano, University of Milano-Bicocca, from October 1999 to December 2003 (n=8562), were considered for the study. Permission to review the patients' records was obtained from the Institutional Review Boards of the 2 institutions.

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Inclusion criteria were availability of the following: (1) both clinic and ABP measurements; (2) ABP recordings of good quality according to predefined criteria (≥80% of valid readings, ≥2 valid measurements per hour during daytime, and ≥1 valid measurement per hour during nighttime); (3) data on age, gender, height, weight, and antihypertensive treatment; and (4) properly filled-in log book reporting working activities during the daytime and sleeping times. Subjects affected by clinically manifest cardiovascular or systemic diseases and those with altered nighttime sleep either because of shift work or because of ABP monitoring (ABPM) were excluded. Likewise, data obtained by repeated ABPM were excluded. Accordingly, we excluded from the study 382 subjects because their ABP recordings covered <20 hours or because a lower than the preset number of measurements was available[8]; 1212 subjects because of incomplete data collection; 382 subjects because their sleep was severely disturbed by the ABP recording; and 182 subjects because ABPM was performed while they were engaged in night work shifts. Therefore, 6404 out of the original 8562 subjects were included in the study (Table I, available online at http://hyper.ahajournals.org). Subjects were considered normotensive when their clinic BP was repeatedly found <140/90 mm Hg and hypertensive when clinic BP was found >140/90 mm Hg over repeated visits or when they were on antihypertensive treatment.

BP Measurements

Clinic BP considered for the study was the average of 2 measurements taken in the sitting position at 5-minute intervals before starting ABP recording.[8] Validated ambulatory devices (SpaceLabs 90207 and Takeda A&D TM-2420)[9,10] were programmed to record BP at 15-minute and 20-minute intervals over the day and the night, respectively.[8] The first 24 hours were processed for analysis, and no editing was performed after data acquisition. Systolic and diastolic ABP and heart rate values were averaged over each hour of the recording, over the day (from 8:00 AM to 8:00 PM), night (from 1:00 AM to 06:00 AM), and over the entire 24-hour period.[8] Morning BP surge was calculated according to Kario et al[11] as the morning systolic BP minus the lowest nighttime systolic BP.

Data From Weather Station

Ta data of the Florence and the Milan areas (°C), obtained from the local office of the National Climatic Data Observatory, were stratified into 3 classes: <10th percentile (−0.7°C to 6.2°C), 10th to 90th (6.2°C to 25.5°C), and >90th (25.5°C to 32.5°C).

Statistical Analysis

Data are expressed as mean±SD. Comparisons between groups were performed using 1-way ANOVA. For multivariate evaluation, age, body mass index (BMI), and Ta were entered in a stepwise multiple regression analysis as independent variables, considering BP (clinic or ambulatory, respectively) or heart rate (clinic or ambulatory) as dependent variables. All of the calculations were performed using the BMDP Statistical Software package. Coefficients of correlation (r) and regression (β) are reported in the tables. A $P<0.05$ was taken as the minimum level of statistical significance throughout the article.

Results

Clinical Characteristics of Study Subjects

The characteristics of subjects fulfilling the inclusion criteria (n=6404) are reported in Table I (available online). The prevalence of hypertension, as well as the allocation to treatment of hypertensive patients, was higher in elderly (O) than in young (Y) subjects ($P<0.02$ and $P<0.001$ at Fisher's exact test, respectively).

Relationship of Outdoor Ta With Blood Pressure and Heart Rate

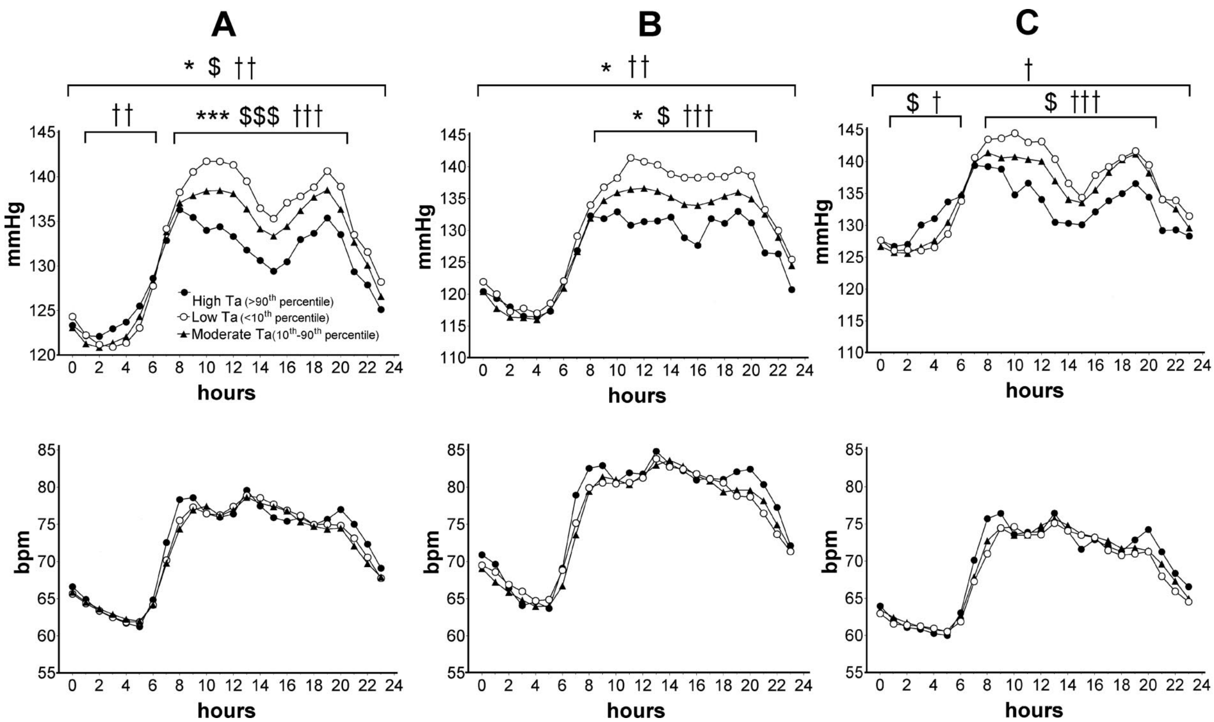
A relatively large number of ABP recordings were performed during every month of the year (>300) in our 2 units. Age and gender distribution, as well as body weight, height, BMI, and smoking habits were comparable in the 3 Ta groups (Table II, available online). As expected, mean daytime systolic and diastolic ABP values were significantly higher during cold days and significantly lower during hot days when compared with those obtained during days with intermediate temperature (P always <0.05; Figure; Table II, available online). During cold days, mean 24-hour systolic ABP, clinic BP, and morning BP surge values (133±11, 141±12, and 37±9 mm Hg, respectively) were also all significantly higher when compared with days with intermediate temperature (132±14 mm Hg, $P<0.05$; 138±18 mm Hg, $P<0.01$; and 35±15, $P<0.01$, respectively) with no differences in nighttime systolic and diastolic ABP values (Figure; Table II, available online). Conversely, during hot days, the nighttime systolic and diastolic ABP values were both significantly higher than those measured in days with intermediate temperature (Figure). In contrast to the Ta dependency of the ambulatory and clinic BP values, both daytime and nighttime heart rate were nonsignificantly different between hot and cold days (Figure; Table II, available online). When BP surge was considered, in the whole group of subjects it displayed a tendency to be greater in cold days as compared with intermediate Ta, but the difference was not statistically significant. Conversely, hot weather was associated with a significant reduction in morning BP elevation (Table II, available online).

At bivariate regression analysis, both clinic and 24-hour ABP were negatively related to Ta ($P<0.01$). When day and night periods were separately considered, Ta displayed a negative relationship with daytime systolic and diastolic BP (SBP and DBP) values and a positive relationship with nighttime BP values (P always <0.01). Multivariate analysis selected Ta as a negative and positive predictor of daytime and nighttime B, P respectively, both for systolic and diastolic values (Table 1). Therefore, in the whole group of subjects, an increase in Ta was associated not only with a significant reduction in clinic, 24-hour, and daytime BP but also with a concomitant increase in night SBP and DBP values, and no relationship was found with heart rate (Table 1).

Effects of Aging

Multivariate analysis selected age as the most important predictor of clinic and ambulatory SBP. A significant but inverse correlation was also found between age and DBP or heart rate values, assessed either in the clinic or over 24 hours (Table 1).

When younger and older subjects were separately considered, in younger subjects no significant modifications either in hot or cold days occurred in the morning BP rise as compared with what was observed with intermediate Ta (33.0±13.9 and 33.7±13.3 mm Hg versus 33.8±13.8 mm Hg, respectively). Conversely, in elderly subjects, the morning BP surge was significantly higher in low than in intermediate Ta (39.5±18.6 mm Hg versus 36.1±16.8 mm Hg; $P<0.01$),



Systolic ABP and heart rate in the whole group of subjects (A), in the subgroup of subjects aged <50 years (B), and in subjects aged >65 years (C) during days with low Ta (Ta <10th percentile; mean daily temperature <6.2°C; ○, n=633, n=153, and n=209, respectively, for the 3 groups), high Ta (Ta >90th percentile; mean daily temperature <25.5°C; ●, n=554; n=110; and n=171) or intermediate Ta (▲, n=5217, n=1167, and n=1811, respectively). *$P<0.05$; **$P<0.01$; ***$P<0.001$ low vs intermediate Ta; $$P<0.05$; $$$P<0.01$; $$$$P<0.001$ high vs intermediate Ta; †$P<0.05$; ††$P<0.01$; †††$P<0.001$ high vs low Ta.

whereas no significant attenuation of this phenomenon was seen in hot days (33.8±17.8 mm Hg), in spite of a persisting pronounced BP increase during the last hours of the night (Figure). Clinic SBP, as well as daytime SBP, showed a significant inverse relationship with Ta in both the Y ($P<0.05$ and $P<0.01$, respectively) and O group (P always <0.01) at bivariate analysis. Conversely, no significant correlation of BP or heart rate with Ta was found in either the Y or O subjects. At multivariate stepwise regression analysis, Ta was selected as a negative independent predictor of clinic SBP in both age groups. Interestingly, Ta was selected as an independent predictor of day and night SBP and DBP only in the O group, displaying a negative and positive relationship with day and night values, respectively (Table 1). Again, no relationship was found between Ta and heart rate in both the Y and O groups.

Effects of Hypertension and Antihypertensive Treatment

To investigate the possible role of hypertension and antihypertensive treatment on Ta-related changes in 24-hour BP profiles, the relationship between Ta and ABP values was separately analyzed in normotensives and in treated and untreated hypertensives. Ta was selected as an independent positive predictor of both systolic and diastolic nighttime ABP values in only the group of treated hypertensives (Table 2). In the same group, Ta was also a negative predictor of daytime ABP values (Table 2). No relationship was found between Ta and heart rate at multivariate analysis in any of the 3 groups.

Combined Effects of Age and Antihypertensive Treatment

In order to discriminate the respective effects of age and treatment on Ta-induced nocturnal ABP increase, the relationship between Ta and nighttime ABP values in the Y and O groups of treated and untreated hypertensive subjects was separately explored by multivariate analysis. Ta was selected as an independent predictor of nighttime systolic ABP only in the O group of subjects receiving antihypertensive treatment (Table 3).

This result was confirmed by the separate analysis of ABP recordings performed during hot and cold days. In particular, nighttime ABP was significantly higher during hot days than during cold days in only the group of elderly subjects treated with antihypertensive drugs (134±16 versus 129±17 mm Hg; $P<0.05$), whereas no differences were found in the untreated elderly subjects (131±15 versus 127±18 mm Hg; P value not significant). No Ta-related BP differences were found between treated and untreated subjects in the Y group. In treated hypertensives >65 years of age, the number of antihypertensive drugs assumed per day was significantly lower in hot than in cold days (1.71±0.86 versus 2.30±1.31 mm Hg; $P<0.001$), whereas no differences were found in hypertensives aged <50 years (1.48±0.72 versus 1.67±0.86 mm Hg; P value not significant).

Discussion

Our study for the first time provides evidence of the following: (1) hot weather is associated not only with a reduction of clinic and daytime BP but also with an increase of nighttime BP values; (2) Ta-related ABP changes are more evident in

TABLE 1. Variables Selected at Multivariate Stepwise Multiple Regression as Independent Predictors of Clinic and Ambulatory SBP and DBP in the Whole Group, in Subjects Aged <50 Years, and in Subjects Aged >65 Years

		Clinic		24-Hour		Nighttime		Daytime	
BP	Variables	r	β	r	β	r	β	r	β
Whole group									
SBP	Age	0.142	0.196	0.139	0.096	0.276	0.273	...	
	BMI	...	...	...	...	...		−0.047	0.106
	Ta	0.050	−0.128			0.085	0.149	−0.078	−0.097
	Clinic SBP	n.i.		0.748	0.553	0.574	0.483	0.779	0.601
	Multiplier r	0.151		0.760		0.627		0.782	
DBP	Age	−0.150	−0.156	−0.221	−0.113	−0.045	−0.029	−0.277	−0.148
	Ta	...	...	...	...	0.060	0.073	−0.068	−0.064
	Clinic DBP	n.i.		0.698	0.467	0.534	0.400	0.723	0.517
	Multiple r	0.173		0.722		0.545		0.753	
Subjects aged <50 years (n=1430)									
SBP	Ta	−0.086	0.196	...	...	...	...	−0.085	0.096
	Clinic SBP	n.i.		0.780	0.601	0.639	0.522	0.784	0.630
	Multiple r	0.086		0.780		0.639		0.788	
DBP	Age	0.102	0.180	0.165	0.146	0.189	0.222	0.157	0.147
	Clinic SBP	n.i.		0.723	0.523	0.581	0.478	0.731	0.549
	Multiple r	0.102		0.735		0.606		0.743	
Subjects aged >65 years (n=2191)									
SBP	Age	0.0721	0.280	0.132	0.252	0.181	0.505	...	...
	Ta	−0.0780	0.216	...	...	0.068	0.133	−0.115	0.153
	Clinic DBP	n.i.		0.733	0.525	0.527	0.438	0.776	0.585
	Multiple r	0.107		0.740		0.552		0.780	
DBP	Age	0.108	0.294	0.116	0.141	...	...	−0.144	−0.183
	Ta	...	...	...	...	0.073	0.087	−0.093	−0.087
	Clinic DBP	n.i.		0.689	0.422	0.498	0.339	0.726	0.488
	Multiple r	0.108		0.698		0.500		0.738	

n.i. indicates variable not included.

the elderly; and (3) in particular, a significant increase in nighttime BP during hot days occurs in elderly subjects treated with antihypertensive drugs. Our study has some important merits, when compared with previous articles, in investigating the effects of Ta on BP. First, both clinic and ABP measurements were considered; and, second, the actual Ta of the days when BP measurements were performed was precisely assessed, rather than more vaguely referring to an entire seasonal period.[1,12,13]

Several previous articles have, indeed, shown that clinic BP undergoes seasonal variations with lower values in summer and higher values in winter months.[14,15] A signifi-

TABLE 2. Variables Selected at Stepwise Multiple Regression as Independent Predictors of Nighttime SBP and DBP in Normotensives (n=1025) and in Treated (n=4105) and Untreated (n=1274) Hypertensives

	Systolic BP						Diastolic BP					
			Hypertensives						Hypertensives			
	Normotensive		Treated		Untreated		Normotensive		Treated		Untreated	
Variables	r	β	r	β	r	β	r	β	r	β	r	β
Age	0.143	0.106	0.293	0.322	0.198	0.167	−0.197	−0.119	−0.055	0.398	...	...
BMI	0.114	0.300	...	...	...	...	0.191	0.396	...	...	...	...
Ta	...	...	0.086	0.154	...	...	...	...	0.048	0.057	...	...
Clinic BP	0.330	0.380	0.564	0.477	0.616	0.560	0.431	0.256	0.509	0.364	0.524	0.420
Multiple r	0.369		0.626		0.655		0.533		0.532		0.524	

TABLE 3. Variables Selected at Stepwise Multiple Regression as Independent Predictors of Nighttime SBP and DBP and Heart Rate in Untreated and Treated Hypertensives <50 Years (n=483 and n=607, respectively) and >65 Years (n=279 and n=1468, respectively)

		<50 Years				>65 Years			
		Untreated		Treated		Untreated		Treated	
BP	Variables	r	β	r	β	r	β	r	β
SBP	Age	...	...	...	...	...	...	0.184	0.506
	Ta	...	...	...	...	...	...	0.087	0.172
	Clinic SBP	0.579	0.504	0.680	0.555	0.692	0.690	0.525	0.449
	Multiple r	0.609		0.689		0.692		0.550	
DBP	Age	0.285	0.349	0.223	0.277	...	...	...	...
	Ta	...	...	...	...	...	...	0.083	0.099
	Clinic DBP	0.444	0.343	0.625	0.483	0.522	0.404	0.468	0.301
	Multiple r	0.537		0.658		0.522		0.479	
Heart rate	BMI	−0.143	−2.182	0.131	0.317	...	...	...	...
	Ta	−0.223	0.273	...	...	...	...	...	...
	Clinic HR	0.387	0.244	0.425	0.270	0.470	0.341	0.504	0.298
	Multiple r	0.605		0.450		0.477		0.504	

cantly lower daytime ABP during summer than during winter was also found in a large-scale population survey, without focusing, however, on age-related differences.[1] In a small prospective study performed in 25 elderly subjects and 21 young volunteers, seasonal changes in ABP were more pronounced in the aged group.[13] Our study provides data on the occurrence of a significant reduction in daytime BP with increasing Ta as a function of age by considering a much larger group of subjects. The absence of Ta-related changes in daytime heart rate seems to exclude the possible role of differences in physical exercise as a responsible factor. In addition, the participation of other potential confounding factors reported previously to be involved in climate-related ABPM changes, such as differences in smoking habits and in BMI,[12,16] can also be excluded.

A new finding of our study, as compared with previous articles on this issue, is the observation that hot weather may also be associated with a significant increase in nighttime BP values. Multivariate stepwise regression analysis revealed that this relationship was independent from anthropometric data and baseline BP values, whereas it was related to subjects' age. Important alterations in sleep patterns or sleep deprivation[17] can be ruled out in our study, because subjects reporting a deeply altered nocturnal sleep were excluded, and because the increase in nighttime BP during hot weather was unrelated to concomitant changes in heart rate, which conversely characterize sleep deprivation.[17] However, although subjects did not report significant restlessness in their log book, milder sleep problems associated with hot weather cannot be completely excluded.

A previous population-based study failed to observe any significant increase in nighttime BP during summer.[1] However, in this study, "seasonal" differences, rather than differences in the actual Ta of the specific days when ABPM was performed, were considered. Furthermore, the study by Sega et al[1] did not include data from ABP recordings performed in August, when hot days are highly prevalent in our regions and when, because of prolonged subjects' exposure to hot weather, the effects of a higher Ta might have reached a more "steady-state" condition. A significant trend toward an increase in night-time BP with increasing Ta was observed previously in a group of 333 untreated hypertensives.[16] In that study, such a BP increase was no more significant after adjustment for confounding variables including age, sex, race, BMI, and baseline BP.[16] Our study offers clear evidence that the opposite effects of an increase in Ta on daytime and nighttime Ta are related to age.

Another important finding of our study is that weather-related changes in ABP profile may also affect the degree of morning BP surge, with Ta-related modifications being mostly evident in aged subjects. On one side, elderly subjects displayed a pronounced enhancement in morning BP surge with cold weather, whereas on the other side, during hot weather they showed no reduction in morning BP surge, associated with an increase in their nocturnal BP levels. These modifications may be potentially dangerous, because they may adversely affect the risk of cardiovascular events both during winter and summer, through different mechanisms. We have to emphasize that the method used in our study to compute morning BP surge, according to Kario et al,[11] has the strongest prognostic value with regard to stroke incidence as compared with different methods.[11]

In hypertensive subjects under pharmacological treatment, the drop in BP during sleep is importantly affected by the duration over 24 hours of the effects of antihypertensive treatment, especially in the elderly.[18] In our study, the finding of a significant association between nighttime BP and Ta was confined to treated elderly hypertensives. It is, therefore, possible that the practice of down-titration applied to antihypertensive drug regimens in summer, common in countries characterized by hot weather in summertime, might have reduced the duration of treatment effects, resulting in an insufficient 24-hour SBP coverage. The significant reduction in the number of administered drugs in our treated elderly subjects during hot days supports this explanation. The average difference in nighttime BP between hot and cold days in aged subjects is relatively low in absolute terms (6 mm Hg), but its magnitude is large enough to be associated with differences in the incidence of hypertensive cardiovascular complications, as shown in several interventional studies.[19] In particular, although evidence is available that stroke mortality,[20,21] as well as the incidence of all kinds of stroke, and, separately, of intracerebral hemorrhage and cerebral infarction,[22,23] increase during the winter months in middle-aged subjects, these seasonal variations seems to decline with age[24] and to be less pronounced in the elderly than in subjects aged <64 years.[4,22] Thus, the results of our study clearly indicate that the practice of reducing treatment in the summer in the elderly based on low clinic BP values is not good, because it might be responsible for a potentially dangerous increase in night BP.

Study Limitations

We acknowledge that our study has some limitations. First, the study design was cross-sectional, with different subjects being examined in the different months of the year, with the possibility of noise in the assessment of Ta effects on BP. However, the study was large enough to make chance findings less likely. Moreover, subject characteristics were well balanced between groups, in particular with regard to possible confounding factors. In this context, we have to specify that subjects included in our study were referred to us by their family doctor or by insurance companies in the frame of a general assessment of their cardiovascular risk. This allowed us to also include real normotensives (both clinic and ABP within normal limits). In a minority of cases, however, the finding of normal clinic and ABP corresponded with the occasional observation of elevated BP values in their family physician's office, probably because of a white coat effect, which was not confirmed at our clinic visits.

Second, although a down-titration of antihypertensive treatment during summertime was demonstrated by the available clinical records, a quantitative assessment of changes in drug doses in different seasons could not be performed for lack of detailed information in most subjects. This did not prevent, however, a clear demonstration of Ta-related differences in the behavior of ABP between treated and untreated subjects and of a reduced number of antihypertensive drugs taken by hypertensive patients in summertime.

Finally, no information is available regarding the indoor temperature. However, the low prevalence of air-conditioning equipment for residential use in Italy and, in particular, among subjects investigated, allow us to exclude that nighttime Ta may be similar in summer and winter.

Perspectives

Our findings may have clinical implications for the development of target organ damage and cardiovascular complications in hypertensive patients in response to weather changes. Although its prognostic implications remain to be determined, the observed BP increase at night in the elderly might increase the risk for both target organ damage and acute cardiovascular events in this population. This phenomenon might counterbalance the likely favorable effects of a Ta-related reduction in daytime BP, an issue that deserves additional investigation by ad-hoc longitudinal studies.

A second clinical implication of our findings is the additional demonstration provided by our data of the importance of ABPM in assessing BP coverage by treatment over 24 hours, in line with previous reports.[8,25] This is particularly important for assessing nighttime BP changes, given the demonstration that nocturnal BP is the strongest predictor of outcome.[26,27] The need for a more frequent use of ABPM in monitoring the effects of antihypertensive treatment in elderly patients under conditions of extreme climate changes is additionally supported by the observation that a smooth BP reduction by treatment contributes to reduce the cardiovascular damage associated with an inadequate 24-hour BP control, the latter characterized by a reduced or an excessive nocturnal BP fall, a steeper morning BP surge,[11] and, in general, an increase in overall BP variability.[28] Finally, our results also have important implications for epidemiological and population studies, because BP recordings obtained at different Tas might introduce a bias in risk stratification.

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