

Prognostic Value of Office and Ambulatory Blood Pressure Measurements in Pregnancy

Ramón C. Hermida, Diana E. Ayala

Abstract—With the objective to assess the prognostic value of office values as compared with ambulatory monitoring in pregnancy, we analyzed 2430 blood pressure series systematically sampled from 403 untreated pregnant women for 48 consecutive hours every 4 weeks from the first visit to the hospital until delivery. Women were divided into 5 groups: “detected” gestational hypertension, women with office blood pressures $>140/90$ mm Hg after 20 weeks of gestation and hyperbaric index (area of blood pressure excess above the upper limit of a time-specified tolerance interval) consistently above the threshold for diagnosing hypertension in pregnancy; “undetected” gestational hypertension, office values $<140/90$ mm Hg but hyperbaric index above the threshold for diagnosis; normotension, both office values and hyperbaric index below the thresholds for diagnosis; white coat hypertension, women with recorded diagnosis of gestational hypertension but hyperbaric index consistently below the threshold for diagnosis; and preeclampsia, defined as gestational hypertension and proteinuria. Results indicate small and nonsignificant differences in 24-hour mean of ambulatory pressures between “detected” and “undetected” gestational hypertension at all stages of pregnancy, in contrast with highly significant differences between these two groups and normotensive pregnancies. Average office blood pressure values were similar for preeclampsia, “detected,” and “undetected” gestational hypertension. The hyperbaric index was, however, significantly higher for women with preeclampsia after 20 weeks of gestation as compared with all other groups and higher for women with either “detected” or “undetected” gestational hypertension as compared with normotensive pregnant women. The incidence of preterm delivery and intrauterine growth retardation were similar for “detected” and “undetected” gestational hypertension but significantly lower for normotensive women. In pregnancy, the hyperbaric index derived from ambulatory monitoring is markedly superior to office measurements for diagnosis of what should be truly considered gestational hypertension, as well as for prediction of the outcome of pregnancy. (*Hypertension*. 2002;40:298-303.)

Key Words: blood pressure monitoring, ambulatory ■ hypertension, pregnancy ■ preeclampsia
■ blood pressure determination

The diagnosis of gestational hypertension still relies on office blood pressure (BP) measurements and the use of arbitrary constant critical thresholds: 140/90 mm Hg for systolic (SBP)/diastolic BP (DBP) after 20 weeks of gestation in a previously normotensive woman.^{1,2} These clinical BP values, however, have several shortcomings; they provide a measurement that represents only a fraction of the 24-hour BP profile, usually under circumstances that may have a pressor effect, and the technique is fraught with potential errors including instrument defects and examiner technique.^{2,3} Therefore, office BP readings are neither diagnostic of nor a good predictor for the development of hypertension in pregnancy.^{4,5} The use of ambulatory BP monitoring (ABPM) has been suggested as the logical approach to overcoming many of the problems associated with clinical BP measurement.^{6,7}

By the use of ABPM, differences between healthy and complicated pregnancies in the circadian pattern of BP,

previously documented for the second trimester of pregnancy,⁸ can be observed as early as in the first trimester of pregnancy, before the actual clinical diagnosis of gestational hypertension or preeclampsia takes place for the women investigated.⁹ The use of the 24-hour mean of BP does not provide, however, a proper approach for an individualized early diagnosis of hypertensive complications in pregnancy.^{5,8,10} Poor results from the diagnostic test based on mean BP values have led many authors to extrapolate erroneously that ABPM is not a valid approach in pregnancy.¹⁰

The circadian pattern with large amplitude that characterizes BP in healthy pregnancies at all gestational ages⁹ suggests that the constant threshold currently used for diagnosing hypertension in pregnancy should be replaced by a time-specified reference limit reflecting the mostly predictable BP variability.^{6,11} Once the time-varying threshold, given, for instance, by the upper limit of a tolerance interval,¹¹ is available, the hyperbaric index (HBI), as a proper

Received May 15, 2002; first decision June 11, 2002; revision accepted June 26, 2002.

From Bioengineering and Chronobiology Laboratories, University of Vigo, Campus Universitario, Vigo, Spain.

Correspondence to Prof Ramón C. Hermida, Bioengineering and Chronobiology Labs, E.T.S.I. Telecomunicación, Campus Universitario, VIGO (Pontevedra) 36200, Spain. E-mail rhermida@tsc.uvigo.es

© 2002 American Heart Association, Inc.

Hypertension is available at <http://www.hypertensionaha.org>

DOI: 10.1161/01.HYP.0000028978.99648.D0

determinant of BP excess,^{6,12} can be calculated as the total area of any given patient's BP above the threshold. The HBI has been shown to be a better determinant of BP excess than the BP load (percentage of BP values above a constant threshold¹³) for the diagnosis of hypertension in pregnancy. This so-called tolerance-hyperbaric test has already been shown prospectively to provide high sensitivity and specificity for the early identification of subsequent hypertensive complications in pregnancy.⁶

Comparative studies between conventional BP measurement and ABPM indicated a high rate of false-negative and false-positive diagnoses of hypertension in pregnancy.¹⁴ Results also suggested that in order to properly apply ABPM in the diagnosis of complications in pregnancy, a new definition of hypertension should be established.¹⁵ The objective of this prospective study was to evaluate and compare the prognostic value of office BP measurements and ABPM (in particular, the HBI calculated from the data obtained by this technique) in the diagnosis of gestational hypertension. The SBP and DBP at different stages along pregnancy as well as other relevant outcome measures (duration of pregnancy, neonatal weight, intrauterine growth retardation [IUGR], preterm delivery) were compared among groups of pregnant women who were systematically studied by 48-hour ABPM from the first obstetric visit to the hospital until delivery.

Methods

Subjects

We studied 403 (207 primipara) untreated white pregnant women who fulfilled all required criteria for this trial (see below). All women received obstetric care at the Obstetric Physiopathology Unit, Hospital Clínico Universitario, Santiago de Compostela, Spain. Reasons for receiving medical care at this unit include familial or personal history of either gestational hypertension or preeclampsia; chronic hypertension; cardiovascular, endocrine, bleeding, or metabolic disease; a personal history of spontaneous abortion; multiple pregnancy; obesity; and adolescent or middle-aged nulliparous pregnancy (<18 or >35 years). The relative risk of gestational hypertension and preeclampsia in this unit is ≈ 3.5 times that of the general obstetric population in our setting.⁹ Therefore, the expected incidence of delivery by cesarean section, before term delivery and IUGR, is also much higher than that of the general obstetric population, as previously documented.^{9,16} All women participating in this trial were thus highly motivated and of relatively high risk for development of complications in pregnancy; the actual percentage of women with complicated pregnancies in this study does not necessarily reflect, therefore, the actual incidence of hypertension in pregnancy in our setting.

The protocol was designed as a prospective, blind study. Thus, all issues related to ABPM, including handling and preparation of the monitors, individualized explanation about their use to each patient, and processing of the data provided by any given pregnant woman after monitoring, were always carried out by the same member of the research group in one room of the unit. Conventional obstetric examinations of the pregnant women, usually done on the same day just before starting ABPM, were carried out by other members of the research group in different rooms of the unit. Office BP measurements (3 to 6 at each obstetric visit) were always obtained by the same midwife to avoid examiner bias.

Inclusion criteria were absence of any condition requiring the use of antihypertensive medication, maternal age (18 to 40 years), and gestational age (<16 weeks at the time of inclusion). Exclusion criteria were, among others, multiple pregnancy, chronic hypertension, chronic liver disease, any disease requiring the use of anti-inflammatory medication, diabetes or any other endocrine disease

such as hyperthyroidism, and intolerance to ABPM device. Apart from the 403 women providing all required information, 23 subjects who provided <4 profiles of ABPM (5 spontaneous abortions and 18 who withdrew from the trial at the early stages of gestation) were eliminated from the study. The State Ethics Committee of Clinical Research approved the study. All women signed consent forms before entering the study.

Women were divided for comparative purposes into 5 groups, taking into account, on the one hand, the recorded diagnosis provided in each woman's personal record by the obstetricians and, on the other hand, the results from monthly ABPM: (1) "detected" gestational hypertension (DGH, $n=65$), women with recorded diagnosis of gestational hypertension (thus defined on the basis of office BP values >140/90 mm Hg for SBP/DBP after 20 weeks of gestation) and HBI consistently above the previously established threshold for diagnosing hypertension in pregnancy⁶ from all ABPM profiles obtained after 20 weeks of gestation; (2) "undetected" gestational hypertension (UGH, $n=63$), here defined as women with office BP values <140/90 mm Hg along gestation and accordingly classified as normotensive by the obstetricians but with HBI consistently above the threshold for diagnosing gestational hypertension from all ABPM profiles obtained after 20 weeks of gestation; (3) normotension ($n=222$), women with both office BP values and HBI below the corresponding thresholds for diagnosing gestational hypertension; (4) "white coat" hypertension (WCH, $n=13$), women with recorded diagnosis of gestational hypertension but with HBI consistently below the threshold for diagnosing gestational hypertension from all ABPM profiles obtained after 20 weeks of gestation; and (5) preeclampsia ($n=40$), defined as gestational hypertension (corroborated by both conventional measurements as well as by HBI) and proteinuria, that is, >300 mg in 24 hours of urine collection, with or without edema, diagnosed after the 20th week of gestation in a previously normotensive woman. The demographic characteristics of the women investigated are included in the Table.

BP Assessment

In this trial, the SBP and DBP of each woman were scheduled to be measured by ABPM every 20 minutes during the day (7 AM to 11 PM) and every 30 minutes during the night for 48 consecutive hours with a SpaceLabs 90207 device at the time of recruitment (usually within the first trimester of pregnancy) and then every 4 weeks until delivery. Women were assessed while adhering to their usual diurnal activity (9:00 AM to midnight for most)–nocturnal sleep routine. They were instructed to go about their usual activities with minimal restrictions but to follow a similar schedule during the 2 days of ABPM and to avoid the use of medication for the duration of the trial. BP series were eliminated from analysis when the women showed an irregular rest-activity schedule during the 2 days of sampling, an odd sampling with spans of >3 hours without BP measurement, or a night resting span <6 hours or >12 hours. The total number of BP series provided by the 403 women under investigation fulfilling all mentioned requirements set a priori was 2430.

The clinical evaluation of this oscillometric monitor for use in pregnancy according to the standards published by the Association for Advancement of Medical Instrumentation and the British Hypertension Society has been previously established.¹⁷ ABPM was performed in addition to the woman's routine antenatal care, and no person was hospitalized during monitoring. The BP cuff was worn on the nondominant arm, with cuff size determined by upper arm circumference at each study visit. ABPM always started between 10:00 AM and 1:00 PM. During monitoring, each subject maintained a diary listing the times they went to bed at night, woke in the morning, and ate meals; exercise and unusual physical activity; and events and mood/emotional states that might affect BP.

Statistical Methods

Each individual's clock hour BP values were first rereferenced from clock time to hours before and after awakening from nocturnal sleep. This transformation avoided the introduction of bias due to differences among subjects in their sleep/activity routine.¹⁸ BP values

Demographic and Perinatal Characteristics of Women Investigated

Variable	NT (n=222)	FP (n=13)	UGH (n=63)	DGH (n=65)	PE (n=40)	P		
						NT vs FP	UGH vs DGH	NT vs UGH
BP series, n	1311	97	385	415	222			
Age, y	30.4±5.6	30.7±5.1	29.6±5.4	29.9±4.5	31.8±5.0	0.838	0.726	0.506
Weight, kg	62.6±9.0	70.2±14.1	69.7±16.0	78.6±17.2	73.3±12.2	0.006	0.002	<0.001
Height, cm	161.9±5.5	160.6±5.3	162.2±7.1	163.7±7.0	162.5±5.5	0.404	0.194	0.776
Age at menarche, y	12.9±1.4	12.5±1.9	12.2±1.4	12.5±1.2	13.2±1.6	0.366	0.162	0.001
SBP at first visit, mm Hg*	118±9	126±16	122±9	127±10	124±10	0.004	0.006	0.006
DBP at first visit, mm Hg*	65±7	68±8	69±8	71±8	69±10	0.144	0.181	0.002
SBP at last visit, mm Hg*	117±9	121±8	133±7	142±11	147±13	0.090	<0.001	<0.001
DBP at last visit, mm Hg*	66±7	68±7	79±6	84±7	87±9	0.352	<0.001	<0.001
Gestational age at delivery, wk	39.4±1.1	39.3±0.8	38.8±3.4	38.7±3.4	37.7±3.1	0.731	0.909	0.030
Newborn weight, g	3322±445	3481±447	3079±642	3093±624	2967±859	0.217	0.905	0.002
Delivery by cesarean section	18.47%	15.38%	38.09%	35.38%	35.00%	0.780	0.751	<0.001
Intrauterine growth retardation	4.95%	7.69%	15.87%	16.92%	27.50%	0.663	0.873	0.003
Preterm delivery (<37 wk)	3.60%	—	9.52%	9.23%	25.00%	—	0.954	0.045
Newborn Apgar score at								
1 min	8.84±0.84	8.46±1.98	8.65±1.17	8.84±0.84	8.18±2.20	0.180	0.557	0.199
5 min	9.88±0.45	9.85±0.38	9.74±0.68	9.86±0.35	9.24±2.02	0.807	0.320	0.095
10 min	9.98±0.20	9.93±0.28	9.94±0.23	9.98±0.13	9.58±1.77	0.636	0.287	0.360

All values are mean±SD, when appropriate. NT indicates normotension; FP, false positive ("white coat" hypertension); UGH, "undetected" gestational hypertension; DGH, "detected" gestational hypertension; PE, preeclampsia.

*Values correspond to the average of 3 to 6 conventional BP measurements obtained by a midwife for each woman at the times of her first and last (before delivery) visits to the hospital.

were then edited according to commonly used criteria for the removal of outliers and measurement errors.¹⁹ The remaining data were analyzed by the use of Chronolab,²⁰ a software package for biological signal processing by linear and nonlinear least-squares estimation. Each BP series was analyzed by the least-squares fit of a multiple component cosine curve with periods of 24 and 12 hours to determine the 24-hour rhythm-adjusted mean or MESOR (midline estimating statistic of rhythm, defined as the average value of the rhythmic function fitted to the data) and the amplitudes of both components.²¹ This model has been shown to describe sufficiently well the circadian pattern of BP variability in healthy and complicated pregnancies,⁹ despite the fact that other ultradian rhythms can be demonstrated as statistically significant in some but not all pregnant women studied by 48-hour ABPM. Since the data were obtained at an unequidistant sampling rate covering approximately two cycles (48 hours), the MESOR provides a better estimation of the true 24-hour mean than the average of all BP values (usually overestimating the true mean due to the denser sampling during activity). The estimates of the 24-hour mean thus obtained for all BP series were used to compare groups of pregnant women at each gestational stage throughout pregnancy by ANOVA. Additionally, the demographic and perinatal characteristics included in the Table were compared between groups of pregnant women by ANOVA (quantitative variables) or nonparametric χ^2 testing (incidence of complications). The HBI for each synchronized BP series was obtained by numeric integration by comparison with the upper limit of tolerance intervals previously established as a function of gestational age.¹¹ Details of the mathematical procedure for determining the HBI have been previously described.²² The HBI values thus obtained were used in conjunction with the conventional diagnosis based on office BP measurements for grouping the subjects under investigation for comparative purposes, as indicated above.

Results

The baseline demographic characteristics of the 5 groups of pregnant women investigated differed in maternal weight but

not in age or height (Table). Maternal weight was characterized by a continuous linear increase along gestation for all groups of women investigated. There was a significant difference between women with UGH and DGH in maternal weight at the time of inclusion ($P=0.002$) but not in their linear pattern of increasing weight throughout pregnancy ($P=0.573$). Women with DGH are characterized by the highest average weight among all groups of pregnant women, including those who had preeclampsia. Weight was significantly higher in complicated pregnancies as compared with normotensive women at all times during gestation. The comparison of the average of 3 to 6 serial office BP measurements taken by a trained midwife at the time of the first visit to the hospital (inclusion) indicate statistically significant differences between all groups being compared in SBP but similar DBP for women with UGH as compared with those with DGH ($P=0.181$). Normotensive women showed significantly lower DBP values at inclusion as compared with the other 4 groups. Differences, however, were highly significant for both SBP and DBP at the time of the last visit to the hospital among all groups, except between normotensive women and those with WCH (Table).

The comparison of the about-monthly averages of circadian BP MESOR indicates a highly significant BP elevation in women with UGH and DGH as compared with normotensive women and those with WCH at all stages of pregnancy (always $P<0.001$; Figures 1 and 2). In normotensive women and those with WCH, polynomial regression analysis indicates a steady linear decrease in SBP (Figure 1) and DBP (Figure 2) up to the 20th week of pregnancy, followed by an

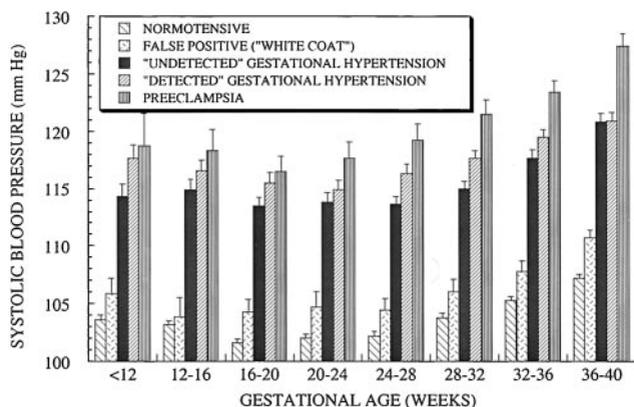


Figure 1. Differences in SBP between groups of pregnant women systematically measured by 48-hour ABPM along gestation.

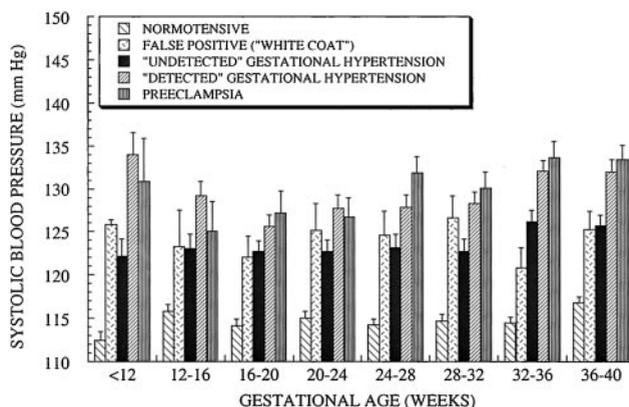


Figure 3. Lack of differences in office SBP values obtained at time of ABPM in groups of pregnant women systematically studied along gestation.

increase in BP up to the day of delivery. This predictable pattern of variation is not found in any of the other 3 groups of pregnant women. For women with UGH, DGH, and preeclampsia, BP is stable until the 22nd week of pregnancy. Between 23 weeks of gestation and delivery, these 3 groups of pregnant women are characterized by a statistically significant increase of BP with gestational age (Figures 1 and 2). Results further indicate that during the first half of pregnancy, SBP is slightly elevated in women who had preeclampsia as compared with those with UGH and DGH ($P=0.011$), but DBP is comparable for these 3 groups of women ($P=0.292$). During the second half of gestation, the linear trend of increasing BP for women who had preeclampsia has a significantly higher slope than the trend for women with UGH or DGH ($P<0.001$ for SBP and DBP). There is no statistically significant difference in SBP or DBP between UGH and DGH at any stage of pregnancy.

The differences between normotensive and hypertensive women in the 24-hour mean of BP shown in Figures 1 and 2 could not be corroborated by office BP measurements. Figure 3 indicates, for SBP, the lack of differences in average conventional BP values determined on the same day before starting ABPM between the groups of women classified as WCH, UGH, DGH, and preeclampsia at all stages of gesta-

tion. Differences among groups were only significant when office BP values obtained for DGH and preeclampsia were compared with those obtained for WCH and UGH after 32 weeks of gestation. Only the women defined as normotensive show average office values significantly lower than the values obtained on the other four groups. A comparison of the distributions of the office BP values obtained for groups of healthy (normotensive and WCH women in the Table) and complicated pregnancies (UGH, DGH, and preeclampsia in the Table) indicates a high degree of overlap (up to 97%) between both groups in all trimesters of pregnancy. The use of these office BP determinations should thus provide a sensitivity in the diagnosis of hypertension in pregnancy below 7% at all stages of gestation. Results for office DBP values (not shown) were similar.

Figure 4 shows the comparison of about-monthly averages of the maximum HBI (maximum of the values obtained for SBP, mean arterial BP, and DBP for each ABPM profile) for the 5 groups of women investigated. Results indicate the lack of differences between normotensive and WCH women, on the one hand, as well as between women here classified as UGH and DGH, on the other hand, at all stages of pregnancy. Women with a final diagnosis of preeclampsia showed HBI values similar to those with gestational hypertension without

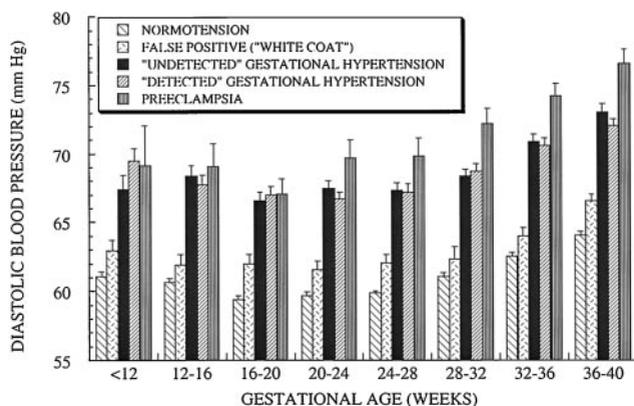


Figure 2. Differences in DBP between groups of pregnant women systematically measured by 48-hour ABPM along gestation.

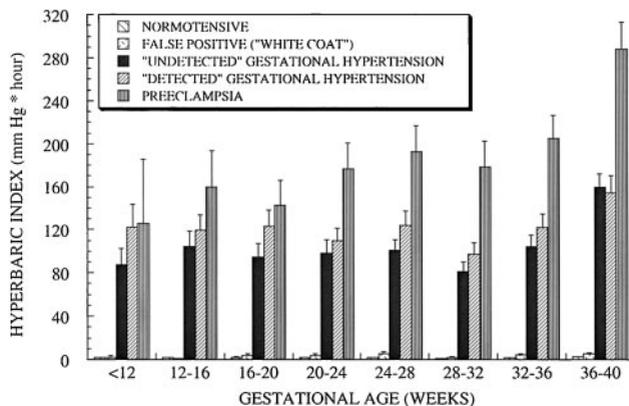


Figure 4. Differences in HBI between groups of pregnant women systematically measured by 48-hour ABPM along gestation.

proteinuria during the first half of pregnancy, in keeping with previous results indicating the lack of BP differences among these two groups during the first and part of the second trimesters of pregnancy.⁹ The average HBI was, however, significantly higher for women who had preeclampsia as compared with all other groups after 20 weeks of gestation ($P < 0.001$; Figure 4). Only 5 of the 1408 ABPM profiles sampled from normotensive or WCH women had an HBI above the previously defined threshold for the diagnosis of hypertension in pregnancy,⁶ whereas all but 3 of the profiles sampled from women with preeclampsia had an HBI always above the threshold. There was no overlap between the distributions of HBI between these two groups of pregnant women after 24 weeks of gestation. Thus, the HBI would provide a 98% sensitivity in the identification of preeclampsia in this study, even during the first trimester of pregnancy. Figure 4 further indicates the lack of differences in HBI between the groups of women defined as UGH and DGH at all stages of pregnancy, as well as the highly significant differences in HBI between these two groups and normotensive or WCH women.

Results from the Table further indicate similar gestational age at delivery between normotensive and WCH women, as well as between women with UGH and DGH. Gestational age at delivery was, however, significantly lower for women with either UGH, DGH, or preeclampsia as compared with the other two groups. Newborns from normotensive women were significantly heavier (almost 250 g on average) than those from women with either UGH or DGH. Normotensive women were also characterized by statistically significant reductions in the incidence of delivery by cesarean section (due to all possible causes), IUGR, and preterm delivery (at < 37 weeks of gestation) as compared with women with UGH or DGH. APGAR scores at 1, 5, and 10 minutes after birth were similar among all groups, with an expected tendency to lower values for newborns from women who had preeclampsia. This later group was also characterized by a significant elevation in the incidence of preterm delivery and IUGR compared with the other 4 groups of women. Delivery by cesarean section was, however, similar for women with preeclampsia, UGH, and DGH. This information may not be as relevant as other parameters included in the Table because total of 62% of the reported cases were due to obesity or cesarean section in the previous pregnancy and thus not specifically related to a diagnosis of hypertension in pregnancy. Results from the Table further indicate that there are no statistically significant differences in any of those perinatal characteristics between normotensive women and those with WCH. More important, there is no statistically significant difference either between UGH and DGH in any studied parameter.

Discussion

Groups of normotensive women and those with UGH, as defined here, do not differ in classification according to the definitions of gestational hypertension adopted by the USA National High Blood Pressure Education Working Group,² by the International Society for the Study of Hypertension in Pregnancy,¹ or by the Australasian Society for the Study of

Hypertension in Pregnancy.^{2,3} According to these standards, gestational hypertension should be applied only to women in the groups defined here as DGH and WCH. In keeping with these definitions of gestational hypertension, women in these two groups were in fact diagnosed with gestational hypertension by the obstetricians participating in this blind study.

By the use of the HBI derived from ABPM, women were also classified as normotensive or hypertensive. Apart from the group with preeclampsia, with an added corroboration of proteinuria in urine collected for 24 hours, the tolerance-hyperbaric test identified as hypertensive those women defined here as UGH and DGH. Results from this prospective trial on women systematically measured by 48-hour ABPM throughout pregnancy indicate highly statistically significant differences in SBP and DBP between pregnant women considered as normotensive and those who showed an HBI consistently above the previously defined threshold for diagnosis of gestational hypertension⁶ after 20 weeks of gestation, independent of their office BP measurements recorded at the hospital. Results from the Table and Figure 3 further indicate that women with UGH have average office BP measurements somehow intermediate between normotensive women and those with DGH, especially at the time of the last visit to the hospital, usually within 1 week before delivery. These differences in office BP values between women with UGH and DGH are no longer significant on the basis of ABPM (Figures 1 and 2).

The comparison of perinatal outcome measures indicate that women defined as normotensive (including those with WCH) are characterized by highly significant reductions of 60% in the incidence of preterm delivery, 70% in the incidence of IUGR, and 50% in the incidence of delivery by cesarean section, as compared with the similar incidence in all those parameters for women with UGH and DGH. Moreover, normotensive women gave birth to children with a significantly higher ($P = 0.002$) average weight of almost 250 g, compared with the newborn weight of children from women with either DGH or UGH. For these later groups, the average newborn weight showed an insignificant difference of 14 g ($P = 0.905$). In summary, groups of women with DGH and UGH are similar in all studied parameters (except maternal weight at the time of inclusion and office BP at the time of delivery), including ABPM throughout gestation. They differ significantly from normotensive women in ambulatory BP values at all stages of pregnancy (Figures 1 and 2) as well as in relevant perinatal measures (Table). Similarity between DGH and UGH also applies to the fact that all women in both groups showed an HBI consistently above the threshold for diagnosis of hypertension in pregnancy for all ABPM sessions carried out after 20 weeks of gestation. These results corroborate the reproducibility of the tolerance-hyperbaric test.¹²

There is actually little agreement concerning the classification of hypertension in pregnancy,²⁴ mostly because different definitions are applied to the diagnosis of preeclampsia. Although preeclampsia has generally received more attention than just hypertension in the absence of any other symptom or complication in pregnancy, the long-term follow-up of women with complicated pregnancies has indicated that

gestational hypertension is the hypertensive disorder of pregnancy with the highest incidence of subsequent chronic hypertension.²⁵ Despite shortcomings of office measurements,³ common to all current classifications is the use of a constant critical threshold for BP obtained at the physician's office for the definition of gestational hypertension. Results from this study corroborate the poor prognostic value of office BP determination for the identification of hypertension in pregnancy. The comparison of the values obtained in this study (Figure 3) indicate the inability of conventional measurements to discriminate between DGH and preeclampsia even in the last stages of pregnancy.

On the other hand, results from this trial further corroborate those from both retrospective and prospective studies indicating that the 24-hour mean of BP does not provide a proper approach for an individualized early diagnosis of hypertensive complications in pregnancy.^{5,8,10} Sensitivity for the detection of gestational hypertension and preeclampsia (that is, discriminating the groups of UGH, DGH and preeclampsia from the groups of normotensive and WCH women) of the 24-hour mean was below 70% at all stages of pregnancy, with specificity as low as 10% for DBP obtained in the first trimester of gestation. The present study corroborates, however, that other indexes obtained from the BP series are useful in identifying early in pregnancy those women in whom subsequent hypertensive complications will develop.⁶ Sensitivity of the HBI in the discrimination of UGH, DGH, and preeclampsia from the other 2 groups was 93% for women sampled during the first trimester of gestation and increased up to 99% in the third trimester. The positive and negative predictive values were >96% in all trimesters. Moreover, results from Figure 4 indicate the ability of the HBI to differentiate women in whom preeclampsia will develop from any other group as early as at 20 weeks of gestation. These results corroborate the potential clinical value of the tolerance-hyperbaric test for the early identification of hypertensive complications in pregnancy.

Whether one should consider as "gestational hypertension" the current accepted definition based on office BP values (that is, women with DGH, or even WCH if this later group is not identified by ABPM) or the definition provided by the reproducible tolerance-hyperbaric test^{6,12} (that is, women with either UGH or DGH as defined here) is a matter of choice, based on personal beliefs. Results from this study do not support office BP measures as a proper "gold standard" for diagnosis of hypertension in pregnancy. These results, in summary, indicate that the HBI, derived from ABPM, is superior to office BP for diagnosis of what should be considered gestational hypertension as well as for prediction of the outcome of pregnancy.

Acknowledgments

This research was supported in part by grants from Dirección General de Enseñanza Superior e Investigación Científica, DGES (PM98-0106); Xunta de Galicia (PGICT99-PXI-32202B and PGICT00-PXI-32205PN); and Vicerrectorado de Investigación, University of Vigo.

References

1. Davey DA, MacGillivray I. The classification and definition of the hypertensive disorders of pregnancy. *Am J Obstet Gynecol.* 1988;158:892-898.
2. National High Blood Pressure Education Program Working Group Report on High Blood Pressure in Pregnancy. *Am J Obstet Gynecol.* 1990;163:1691-1712.
3. Sibai BM. Pitfalls in diagnosis and management of preeclampsia. *Am J Obstet Gynecol.* 1988;159:1-5.
4. Peek M, Shennan A, Halligan A, Lambert PC, Taylor DJ, De Swiet M. Hypertension in pregnancy: which method of blood pressure measurement is most predictive of outcome? *Obstet Gynecol.* 1996;88:1030-1033.
5. Hermida RC, Ayala DE. Diagnosing gestational hypertension and preeclampsia with the 24-hour mean of blood pressure. *Hypertension.* 1997;30:1531-1537.
6. Hermida RC, Ayala DE, Mojón A, Fernández JR, Silva I, Uceda R, Iglesias M. Blood pressure excess for the early identification of gestational hypertension and preeclampsia. *Hypertension.* 1998;31:83-89.
7. Shennan A, Halligan A. Ambulatory blood pressure monitoring in pregnancy. *Fetal Maternal Med Rev.* 1998;10:69-89.
8. Kyle PM, Clark SJ, Buckley D, Kissane J, Coats AJS, De Swiet M, Redman CWG. Second trimester ambulatory blood pressure in nulliparous pregnancy: a useful screening test for pre-eclampsia? *Br J Obstet Gynaecol.* 1993;100:914-919.
9. Hermida RC, Ayala DE, Mojón A, Fernández JR, Alonso I, Silva I, Uceda R, Iglesias M. Blood pressure patterns in normal pregnancy, gestational hypertension and preeclampsia. *Hypertension.* 2000;36:149-158.
10. Higgins JR, Walshe JJ, Halligan A, O'Brien E, Conroy R, Darling MRN. Can 24-hour ambulatory blood pressure measurement predict the development of hypertension in primigravidae? *Br J Obstet Gynaecol.* 1997;104:356-362.
11. Hermida RC, Ayala DE, Mojón A, Fernández JR. Time-qualified reference values for ambulatory blood pressure monitoring in pregnancy. *Hypertension.* 2001;38:746-752.
12. Hermida RC, Fernández JR, Mojón A, Ayala DE. Reproducibility of the hyperbaric index as a measure of blood pressure excess. *Hypertension.* 2000;35:118-125.
13. Hermida RC, Ayala DE. Evaluation of the blood pressure load in the diagnosis of hypertension in pregnancy. *Hypertension.* 2001;38:723-729.
14. Olofsson P, Persson K. A comparison between conventional and 24-hour automatic blood pressure monitoring in hypertensive pregnancy. *Acta Obstet Gynecol Scand.* 1995;74:429-433.
15. Brown MA, Robinson A, Bowyer L, Buddle ML, Martin A, Hargood JL, Cario GM. Ambulatory blood pressure monitoring in pregnancy: what is normal? *Am J Obstet Gynecol.* 1998;178:836-842.
16. Hermida RC, Ayala DE, Iglesias M. Predictable blood pressure variability in healthy and complicated pregnancies. *Hypertension.* 2001;38:736-741.
17. Shennan AH, Kissane J, De Swiet M. Validation of the SpaceLabs 90207 ambulatory blood pressure monitor for use in pregnancy. *Br J Obstet Gynaecol.* 1993;100:904-908.
18. Hermida RC. Time-qualified reference values for 24 h ambulatory blood pressure monitoring. *Blood Press Monit.* 1999;4:137-147.
19. Staessen J, Fagard R, Lijnen P, Thijs L, Vaa Hoof R, Amery A. Ambulatory blood pressure monitoring in clinical trials. *J Hypertens.* 1991;9(suppl 1):s13-s19.
20. Mojón A, Fernández JR, Hermida RC. Chronolab: an interactive software package for chronobiologic time series analysis written for the Macintosh computer. *Chronobiol Int.* 1992;9:403-412.
21. Fernández JR, Hermida RC. Inferential statistical method for analysis of nonsinusoidal hybrid time series with unequidistant observations. *Chronobiol Int.* 1998;15:191-204.
22. Hermida RC, Mojón A, Fernández JR, Ayala DE. Computer-based medical system for the computation of blood pressure excess in the diagnosis of hypertension. *Biomed Instrum Technol.* 1996;30:267-283.
23. Australasian Society for the Study of Hypertension in Pregnancy. Consensus statement: management of hypertension in pregnancy: executive summary. *Med J Aust.* 1993;158:700-702.
24. Brown MA, Buddle ML. What's in a name? Problems with the classification of hypertension in pregnancy. *J Hypertens.* 1997;15:1049-1054.
25. Marín R, Gorostidi M, Portal CG, Sánchez M, Sánchez E, Alvarez J. Long-term prognosis of hypertension in pregnancy. *Hypertens Preg.* 2000;19:199-209.