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Automated blood pressure measurement as a predictor of proteinuric pre-eclampsia

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Objectives To investigate the relation between antenatal clinic, obstetric day unit and 24-hour ambulatory blood pressure measurements and 24-hour proteinuria levels in hypertensive pregnancies.

Design An observational study.

Participants Forty-eight women presenting with new hypertension after 20 weeks of gestation.

Results The closest relation was found between ambulatory blood pressure measurements and 24-hour proteinuria levels. No significant relation was found between the conventional diastolic blood pressure threshold of 90 mmHg and 24-hour proteinuria levels.

Conclusions Ambulatory blood pressure measurement gives better information about disease status in pre-eclampsia as assessed by proteinuria than does conventional sphygmomanometry.

INTRODUCTION

Pre-eclampsia after 20 weeks of gestation is a multisystem syndrome and is associated with a poor fetal outcome[1–3], particularly when presenting remote from term[3,4]. Due to ease of detection and by convention, hypertension and proteinuria have been accepted as the hallmarks of pre-eclampsia. However, blood pressure levels are variable and the blood pressure may be elevated for reasons other than pre-eclampsia. Proteinuria is generally considered a more reliable (though not infallible) sign of pre-eclampsia, just as the degree of proteinuria is likewise perceived to relate to the severity of this condition. The aims of our study were to investigate the relation between antenatal clinic, obstetric day unit and 24-hour automated blood pressure measurements (ABPM) and proteinuria in hypertensive pregnancies, and to find which measurement of blood pressure (if any) related best with the degree of proteinuria.

METHODS

Forty-eight primiparous caucasian women more than 20 weeks pregnant with hypertension (i.e. ≥ 140/90 mmHg averaged on five measurements half an hour apart) confirmed on obstetric day unit underwent a 24-hour urine collection to estimate protein loss. The mean age of the women was 29·4 years (range 17–42) and a mean gestation of 35·5 weeks (range 32–39). Each woman study had been referred from the antenatal clinic because of raised blood pressure. Following recruitment on the obstetric day unit each woman was given a 24-hour automated blood pressure monitor. Obstetric day unit assessment involved five blood pressure measurements taken by conventional sphygmomanometry in relaxed surroundings half an hour apart and arithmetically meaned. Korotkoff phase 4 was used for diastolic blood pressure measurement. Three women had only diastolic blood pressure measured in the obstetric day unit. 24-hour automated blood pressure monitoring involved oscillometric automated blood pressure measurement taken every 30 min throughout the day and night. Particular care was taken with both conventional and automated measurement to ensure that a cuff containing a bladder with dimensions appropriate for the arm circumference was chosen. The pregnancy validated SpaceLabs 90207 (SpaceLabs Medical, Redmond, Washington, USA)[5] was used for 24-hour monitoring of blood pressure. The normal range and patient acceptability for the SpaceLabs 90207 have been established previously in a primiparous caucasian cohort[6]. For the purposes of analysis, daytime was from 07:00 to 22:59 and night-time was from 23:00 to 06:59. The women were thoroughly educated to ensure an optimal 24-hour urine collection. Proteinuria analysis was performed using the COBAS BIO analyser (Roche Analytical Instruments, Nutley, New Jersey, USA) which is a

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Table 1. Median, lower and upper quartiles for each blood pressure measurement and proteinuria.

	n	Lower quartile	Median	Upper quartile
Systolic (mmHg)				
Clinic	47	137·5	140	141·5
Day unit	44	135	140	148·5
ABPM day	47	128·5	136	146
ABPM night	47	116	123	136
Diastolic (mmHg)				
Clinic	47	90	95	100
Day Unit	47	87·5	90	97·5
ABPM day	47	83·5	89	94·5
ABPM night	47	68·5	78	83·5
Proteinuria (g)	47	0·36	0·46	0·8

Table 2. Results of linear regression analyses for the relation between blood pressure and (log) proteinuria. Values in parentheses are standard errors.

	Intercept	Gradient	R^2	*P*
Systolic (mmHg)				
Clinic	142·1 (1·83)	1·07 (1·80)	0·01	0·56
Day unit	142·3 (2·23)	0·77 (2·21)	0·00	0·73
ABPM day	138·1 (1·87)	4·24 (1·84)	0·11	0·026
ABPM night	128·9 (2·21)	6·68 (2·17)	0·17	0·004
Diastolic (mmHg)				
Clinic	96·2 (1·20)	0·37 (1·18)	0·00	0·76
Day unit	91·8 (1·39)	1·87 (1·37)	0·04	0·18
ABPM day	90·7 (1·47)	4·65 (1·44)	0·19	0·002
ABPM night	80·8 (1·64)	5·97 (1·61)	0·23	< 0·001

single unit, self-contained, centrifugal analyser which utilises the horizontal light path principle. The precision of this technique is well established[7]. Quality assurance was performed prior to each analysis.

Proteinuria displayed a skewed distribution and was logged for purposes of analysis. Without logging the data, any relation observed could be influenced by high values of proteinuria. The relation between the four measures of blood pressure and log proteinuria was assessed using linear regression by performing four separate analyses for both systolic and diastolic blood pressure. In order to assess whether the four gradients obtained from the linear regression analyses were statistically significant from each other, a two-level multivariate model was fitted[8].

RESULTS

Table 1 shows the median, lower and upper quartiles for each variable. For both systolic and diastolic blood pressure, ambulatory blood pressure measurement has a lower median than either the clinic or day unit, most noticeably at night.

Table 2 shows the relation between both the four systolic and the four diastolic blood pressures and log proteinuria. For systolic blood pressure there was little relation between either the antenatal clinic or the obstetric day unit measures and log proteinuria. In addition, inspection of the data showed observer bias in the form of terminal digit preference, especially for the antenatal clinic measure. Both the daytime ($P = 0{\cdot}026$) and night-time ($P = 0{\cdot}004$) ambulatory blood pressure measurements show a significant positive relation with log proteinuria, with the night-time measure having the steepest gradient (i.e. for each unit increase in log proteinuria, night-time systolic blood pressure has a larger increase than daytime systolic blood pressure). Formal testing of the four gradients via the two-level model indicated that there were significant differences between them ($\chi^2_3 = 8{\cdot}75$, $P = 0{\cdot}033$).

Similar results were observed for diastolic blood pressure, with little relation between the antenatal clinic or obstetric day unit measure and log proteinuria. Again, terminal digit preference was observed. There was a positive significant relation between both the daytime ($P = 0{\cdot}002$) (Fig. 1) and night-time ($P < 0{\cdot}001$) (Fig. 2) ambulatory blood pressure measurements with again the largest gradient observed for the night-time measure. Formal testing of the four gradients indicated that there were significant differences between them ($\chi^2_3 = 8{\cdot}97$, $P = 0{\cdot}030$).

DISCUSSION

The purpose of this study was to investigate the relation between 24-hour proteinuria excretion and blood pressure parameters in pregnant women identified as hypertensive after 20 weeks of gestation. None of the four parameters based on conventional sphygmomanometry attained statistical significance. In particular, the least statistically significant correlation was with diastolic blood pressure as measured at the antenatal clinic in the conventional manner. Yet, this traditional measurement has been conventionally used for the diagnosis and classification of hypertensive disorders of pregnancy[9–11]. The best correlates for systolic and diastolic blood pressure and 24-hour proteinuria were noted with day and, in particular, night-time ambulatory blood pressure measurements.

It is generally agreed that pre-eclampsia is a multisystem disorder with hypertension as an easily measurable, though secondary sign[12,13]. Proteinuria is another manifestation of this condition. It reflects both the pathognomonic glomerular endotheliosis lesion and a generalised increase in capillary permeability[14–16]. Conventional urine analysis by dipstick is subject to

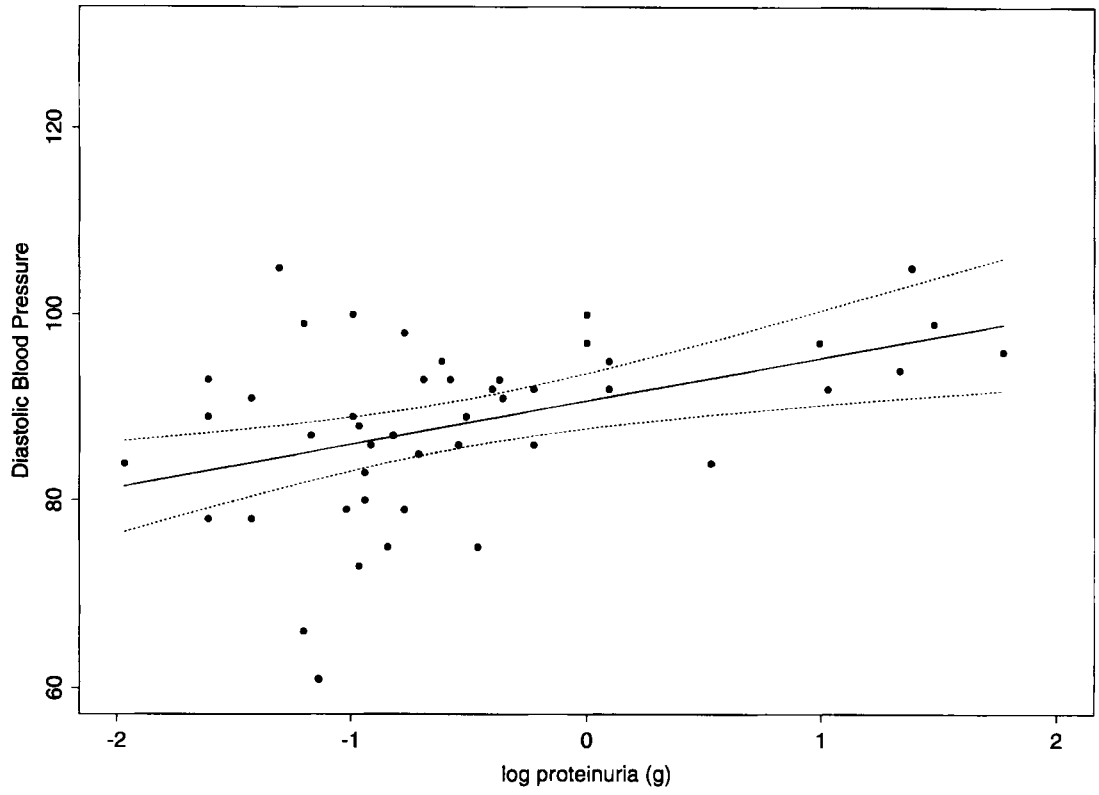

Fig. 1. Diastolic ambulatory blood pressure measurement day measure.

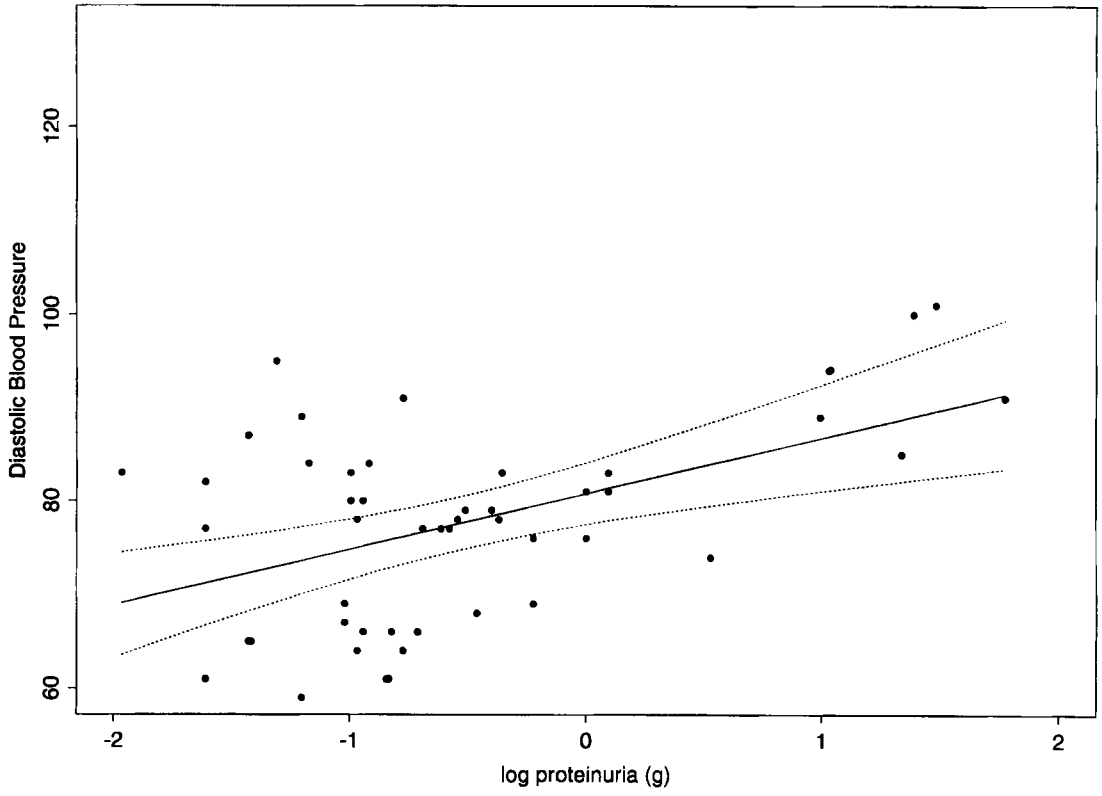

Fig. 2. Diastolic ambulatory blood pressure measurement night measure.

great variability[2,17,18]. For these reasons, we used 24-hour proteinuria levels. We have been unable to find any studies which have shown a significant relation between blood pressure measurement and levels of proteinuria. Indeed, significant proteinuria has been documented in women found to be normotensive who subsequently developed eclampsia[19]. The basis for designating these women as normotensive, however, was that conventional diastolic blood pressures did not exceed the accepted thresholds. It is not clear which of the many differences between automated blood pressure measurement and conventional sphygmomanometry account for the superiority of automated measurement to predict proteinuria (i.e. whether it is the multiple, automated readings or whether it is measurement away from the hospital environment). By measuring blood pressure using automated monitoring, our findings indicate that cardiovascular and renal signs of pre-eclampsia are not independent but may be interlinked. The fact that blood pressure and proteinuria are related suggests that automated blood pressure measurement gives better information about the disease status in pre-eclampsia.

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