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What is hypertension in diabetes? Ambulatory blood pressure in 137 normotensive and normoalbuminuric Type 1 diabetic patients

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Abstract

Aims To establish reference data for ambulatory blood pressure (AMBP) in normotensive, normoalbuminuric Type 1 diabetic patients and characterize the relation to clinic blood pressure (BP). To evaluate the statement of the third working party of the British Hypertension Society (BHS) that a target clinic BP in diabetes < 140/80 corresponds to a target day-time AMBP < 130/75 mmHg.

Patients and methods AMBP were performed in 172 normoalbuminuric, adult Type 1 diabetic patients, who had never received anti-hypertensive drugs. Clinic BP was determined as the mean of at least three auscultatory (Hawskley random zero manometer) and as the mean of at least three oscillometric (Spacelabs) BP values obtained just prior to ambulatory monitoring. Five patients with more than three missing hours/24 h were excluded.

Results For 30 patients auscultatory clinic BP exceeded 140 mmHg systolic and/or 90 mmHg diastolic. For the remaining 137 normotensive patients day-time AMBP was 125.7/77.2 mmHg and oscillometric clinic BP was 125.3/76.5 mmHg (mean difference 0.3/0.7 mmHg; 95% confidence interval (CI) –0.9 to 1.5/–0.3 to 1.7 mmHg, $P = 0.6$/$P = 0.2$). Sixty-five percent of the patients had a diastolic day-time AMBP > 75 mmHg.

Conclusions Clinic BP and day-time AMBP measured by the same method were indistinguishable. The target for day-time diastolic AMBP (< 75 mmHg) proposed by the BHS is too low and is based on the misconception that in normotensive subjects day-time AMBP is lower than clinic BP. If the BHS guidelines are strictly adhered to, the consequence may be overtreatment in patients with normoalbuminuria and no end organ damage.

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Keywords ambulatory blood pressure, diabetes, hypertension

Abbreviations AMBP, ambulatory blood pressure; BP, blood pressure; BHS, British Hypertension Society; ISH, International Society of Hypertension

Introduction

Ambulatory blood pressure (AMBP) monitoring is now approved by several Institutions including the British Hypertension Society (BHS) and guidelines provided [1,2]. The third working party of the BHS states that target

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clinic blood pressure (BP) for diabetic patients is < 140/80 mmHg and that the corresponding target day-time AMBP is < 130/75 mmHg [1]. We are concerned about the recommendations for AMBP, in particular the suggestion of a diastolic day-time AMBP < 75 mmHg. We here report data of AMBP from 137 normotensive and normoalbuminuric Type 1 diabetic patients.

Patients and methods

Adult Type 1 diabetic patients (age 18–60 years) without previous anti-hypertensive treatment were included if geometric mean of three overnight urinary albumin (RIA) excretions was < 20 μg/min (n = 172) [3,4]. The studies were approved by the local ethics committee and patients gave their informed consent. Spacelabs monitor model 90207 or 90202 operating by oscillometry was used [5,6]. After demonstration of the equipment at least two oscillometric BP measurements were performed for familiarization. Simultaneous auscultatory and oscillometric measurements are not feasible because of the fast stepwise deflation of the cuff pressure [7]. Therefore clinic BP was measured by a sequential technique on the left arm. Four oscillometric and four interposed auscultatory measurements (Hawskley random zero manometer) were performed (for 90202 three measurements by each method) with the patients in the sitting position and the arm supported. The auscultatory and oscillometric clinic BP were calculated as the average of these measurements. Ambulatory recordings were performed every 20 min for 24 h (for 90202 every 60 min from 24.00 to 06.00). Day and night AMBP were calculated from hourly average values according to individual records of time for retiring and rising. HbA_{1c} was determined with high performance liquid chromatography (HPLC) (non-diabetic range 4.4–6.4%). Differences in BP were tested by Student's paired t-test. Limits of agreement between oscillometric and auscultatory methods were assessed as the mean ± 1.96 × SD of the difference between the methods [8].

Table 1 Clinical data for 137 normotensive and normoalbuminuric Type 1 diabetic patients

Male/female	76/61
Age (years)	35.4 ± 9.7
Body mass index (kg/m^2)	23.6 ± 2.4
Smoker (no/yes)	90/47
Diabetes duration (years)	17.9 ± 9.3
HbA_{1c} (%)	8.3 ± 1.2
Urinary albumin excretion (μg/min)	4.5 × /÷ 1.7
Patients with 0/1/2/3 missing AMBP hours	113/19/4/1
AMBP on work day (no/yes/unreported)	84/50/3
Spacelabs 90207/90202	75/62

Data are numbers, mean ± SD or geometric mean × /÷ tolerance factor.

Results

Five patients with more than three missing hours were excluded and 30 patients were excluded because auscultatory clinic BP was > 140 systolic and/or > 90 diastolic mmHg. Clinical characteristics and BP data of the remaining 137 normotensive patients are presented in Tables 1 and 2. Sixty-five percent of the patients had diastolic day-time AMBP > 75 mmHg and 27% had a diastolic day-time AMBP > 80 mmHg. Thirty percent of the patients had systolic day-time AMBP > 130 mmHg and 15% had systolic day-time AMBP > 135 mmHg.

Day-time AMBP vs. clinic BP

The mean systolic difference (day-time AMBP – oscillometric clinic BP) was 0.3 mmHg (95% confidence interval (CI) –0.9 to 1.5; P = 0.58) and 0.7 mmHg for diastolic BP (95% CI –0.3 to 1.7; P = 0.17).

Systolic night/day ratio was significantly higher than diastolic night/day ratio (mean difference 0.064, 95% CI 0.057–0.071; P < 0.001).

Table 2 Blood pressure for 137 normotensive and normoalbuminuric Type 1 diabetic patients

	Mean BP ± SD (systolic/diastolic)	90, 95 percentile (systolic/diastolic)
Clinic BP (auscultatory, Hawskley, mmHg)	117.4 ± 10.0/77.8 ± 7.2	132/87, 135/89
Clinic BP* (oscillometric, Spacelabs, mmHg)	125.3 ± 9.6/76.5 ± 7.0	139/85, 144/86
Day-time AMBP (oscillometric, Spacelabs, mmHg)	125.7 ± 8.1/77.2 ± 5.7	137/85, 140/87
Night-time AMBP (oscillometric, Spacelabs mmHg)	110.8 ± 8.2/63.1 ± 6.2	122/71, 125/74
Night/day ratio	0.88 ± 0.05/0.82 ± 0.07	0.95/0.90, 0.97/0.94
24-h AMBP (oscillometric, Spacelabs mmHg)	120.8 ± 7.5/72.6 ± 5.4	131/80, 134/82

†n = 136.

Oscillometric vs. auscultatory clinic BP

The mean systolic difference (oscillometric clinic BP – auscultatory clinic BP) was 8.0 mmHg (95% CI 7.0–8.9, $P < 0.001$; 95% limits of agreement –3.1 to 19.0 mmHg). The mean diastolic difference was –1.3 mmHg (95% CI –2.2 to –0.4, $P < 0.01$; 95% limits of agreement –11.7 to 9.2 mmHg).

Discussion

Day-time AMBP and clinic BP were indistinguishable in normotensive normoalbuminuric diabetic patients. This result was not influenced by any systematic difference between the two methods for BP measurement since clinic BP and day-time AMBP for comparison were measured with the same monitor, in contrast to previous studies [9]. Two-thirds of the normotensive patients have a diastolic day-time AMBP above the suggested target for anti-hypertensive treatment (< 75 mmHg). This recommendation seems inappropriate if applied to patients without abnormal albuminuria or other signs of organ damage, and may lead to overtreatment if strictly adhered to. The guidelines of the third working party of BHS state that AMBP is systematically lower than clinic measurements in hypertensive and normotensive subjects [1]. It is well known that day-time AMBP is lower than clinic BP in clinic hypertensive subjects [9]. However, for normotensive subjects the opposite phenomenon is usually seen, i.e. a slightly higher or similar day-time to clinic value, as documented in our study. In a large population-based study, clinic BP in normotensive subjects was 119/73 mmHg and day-time AMBP was 122/75 mmHg ($n = 4577$) [9]. This may be explained by the exclusion of subjects with isolated clinic hypertension and the effect of AMBP measurement on a work day compared with a clinic BP in the relaxed subject. The third working party of BHS also state that precise adjustment is complex, but the average difference between clinic and day-time AMBP is approximately 12/7 mmHg [1]. Although this may be a useful rule in patients with elevated clinic BP, this correction can not be applied to clinic BP in the normal range. Similar objections have been presented against the WHO/International Society of Hypertension (ISH) suggestions of a target day-time AMBP < 120/80 mmHg [10].

Our study is not a validation study, but our results confirm previous observations of an overestimation by the Spacelabs monitor of systolic BP in the (low) normal range [11]. This emphasizes that comparison of clinic and ambulatory BP should employ similar methodology. In addition, normal data and suggestions of targets may unfortunately be valid only for the specific monitor employed. The importance of systematic differences between auscultatory and automatic monitors has recently been underscored by the HOT study [12]. In this study clinic BP was measured exclusively by the Visomat OZ oscillometric equipment, which by subsequent validation was shown to underestimate significantly the systolic BP by 6.4 mmHg and the diastolic BP by 0.9 mmHg [13]. While the reported association between low target BP and reduced complications in diabetic patients is unaffected, the suggested target clinic BP values (for auscultatory BP) should be interpreted accordingly.

Although no consensus exists, non-dippers are usually defined as subjects with a reduction of both systolic and diastolic AMBP < 10% of the day-time average [14] (i.e. a systolic and diastolic night/day ratio > 0.90). Since systolic night/day BP ratio is higher than the diastolic ratio in most studies [15,16], we advocate a definition of non-dipping which states that both systolic and diastolic night/day ratio should be > the 90th percentile level, which in the present study (employing individual determined night periods) is reported to be 0.95 for systolic and 0.90 for diastolic night/day BP ratio.

Goals for AMBP should be based on intervention studies demonstrating protection against end organ damage [17]. Until such data are available recommendations must rely on information about normal data of AMBP and the association between clinic and ambulatory BP. In our study the upper limit of normality (95th percentile) for day-time AMBP was 140/87 mmHg, which closely matches the value 138/87 mmHg reported in population-based studies of normotensive subjects [16]. Against this background a consensus conference has proposed operational thresholds for abnormality (> 140/90) and normality (< 135/85 mmHg) of day-time AMBP [17]. These standards have been adopted by BHS in a very recent recommendation [2]. It is not quite clear if the cut off value 135/85 mmHg for normal day-time AMBP also represents the suggested level for initiation of anti-hypertensive therapy or the goal for such therapy. The paper states that 'lower values cannot be recommended unless evidence from ongoing longitudinal studies indicate otherwise'; however, day-time AMBP < 135/85 mmHg 'may be abnormal in patients whose total risk factor profile is high and in whom there is a concomitant disease' such as diabetes or target organ damage [2].

The target values for clinic BP in normoalbuminuric patients proposed by the third working party of BHS (< 140/80 mmHg) and by the European Diabetes Policy Group (< 140/85 mmHg for Type 2 diabetes, < 135/85 mmHg for Type 1 diabetes) represent higher systolic values than suggested by the American Diabetes Association, the Joint National Committee on Prevention, Evaluation and Treatment of High Blood Pressure and WHO/ISH (< 130/85 mmHg) [18–22]. If the higher target value for systolic clinic BP (< 140 mmHg) in diabetic patients proposed by the third working party of BHS is accepted, we suggest that a corresponding target for systolic day-time AMBP value should be < 135 mmHg to

follow recommendations of normality [2,17], which equals the 85th percentile level in normotensive patients in our study. Suggestions of a lower systolic target (in patients with normoalbuminuria and without end organ damage) could come from observational studies [23–25] but should ideally be based on intervention studies. The concept of BP targets in diabetes can be criticized because of the lack of threshold in observational studies [25] but is still considered of practical value. If the target value for diastolic clinic BP (< 80 mmHg) is accepted, we suggest day-time AMBP should be < 80 mmHg to acknowledge the fact that clinic BP in the normotensive range is very close to the day-time average, as demonstrated in the present study.

References

1 Ramsay LE, Williams B, Johnston GD, MacGregor GA, Poston L, Potter JF *et al*. Guidelines for management of hypertension: report of the third working party of the British Hypertension Society. *J Hum Hypertens* 1999; **13:** 569–592.

2 O'Brien E, Coats A, Owens P, Petrie J, Padfield PL, Littler WA, de Swiet M, Mee F. Use and interpretation of ambulatory blood pressure monitoring: recommendations of the British Hypertension Society. *BMJ* 2000; **320:** 1128–1134.

3 Hansen KW. Ambulatory blood pressure in insulin-dependent diabetes: the relation to stages of diabetic kidney disease. *J Diabetes Complications* 1996; **10:** 331–351.

4 Poulsen PL, Ebbehøj E, Hansen KW, Mogensen CE. 24-h blood pressure and autonomic function is related to albumin excretion within the normoalbuminuric range in IDDM patients. *Diabetologia* 1997; **40:** 718–725.

5 O'Brien E, Mee F, Atkins N, O'Malley K. Accuracy of the SpaceLabs 90207 determined by the British Hypertension Society Protocol. *J Hypertens* 1991; **9:** S25–S31.

6 O'Brien E, Mee F, Atkins N, O'Malley K. Evaluation of the SpaceLabs 90202 non-invasive ambulatory recorder according to the AAAMI standard and the BHS criteria. *J Hum Hypertens* 1991; **5:** 223–226.

7 O'Brien E, Petrie J, Littler W, de Swiet M, Padfield PL, Altman DG *et al*. The British Hypertension Society protocol for the evaluation of blood pressure measuring devices. *J Hypertens* 1993; **11:** S43–S62.

8 Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; **i:** 307–310.

9 Staessen JA, O'Brien ET, Atkins N, Amery AK. Ambulatory blood pressure in normotensive compared with hypertensive subjects. *J Hypertens* 1993; **11:** 1289–1297.

10 O'Brien E, Staessen JA. What is 'hypertension'? *Lancet* 1999; **353:** 1541–1543.

11 Pexioto AJ, Gray TA, Crowley ST. Validation of the SpaceLabs 90207 ambulatory blood pressure device for hemodialysis patients. *Blood Press Monit* 1999; **4:** 217–221.

12 Hansson L, Zanchetti A, Carruthers SG, Dahlöf B, Elmfeldt D, Julius S *et al*. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) Study randomised trial. *Lancet* 1998; **351:** 1755–1762.

13 Lithell H, Berglund H. Validation of an oscillometric blood pressure measuring device: a substudy of the HOT study. *Blood Pressure* 1998; **7:** 149–152.

14 Verdecchia P, Schillaci G, Porcellati C. Dippers versus non-dippers. *J Hypertens* 1991; **9:** S42–S44.

15 Staessen JA, Bieniaszewski L, O'Brien E, Gosse P, Hayashi H, Imai Y *et al*. Nocturnal blood pressure fall on ambulatory monitoring in a large international database. *Hypertens* 1997; **29:** 30–39.

16 Staessen JA, O'Brien ET. Development of diagnostic thresholds for automated measurements of blood pressure in adults. *Blood Press Monit* 1999; **4:** 127–136.

17 Staessen JA, Beilin L, Parati G, Waeber B, White W. Task force IV: Clinical use of ambulatory blood pressure monitoring. *Blood Press Monit* 1999; **4:** 319–331.

18 European Diabetes Policy Group. A desktop guide to Type 2 diabetes mellitus 1999. *Diabetic Med* 1999; **16:** 716–730.

19 European Diabetes Policy Group. A desktop guide to Type 1 (insulin-dependent) diabetes mellitus, 1998. *Diabetic Med* 1999; **16:** 253–266.

20 American Diabetes Association. Standards for medical care for patients with diabetes mellitus. *Diabetes Care* 2000; **23:** S32–S42.

21 The Joint National Committee of Prevention, Detection, Evaluation and Treatment of High Blood Pressure. The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of high Blood Pressure. *Arch Intern Med* 1997; **157:** 2443–2446.

22 Guidelines Subcommittee. 1999 World Health Organization–International Society of Hypertension Guidelines for the management of Hypertension. *J Hypertens* 1999; **17:** 151–183.

23 Staessen JA, Thijs L, Fagard R, O'Brien ET, Clement D, Leeuw PW *et al*. Predicting cardiovascular risk using conventional vs ambulatory blood pressure in older patients with systolic hypertension. *JAMA* 1999; **282:** 539–546.

24 Stamler J, Vaccaro O, Neaton JD, Wentworth D. Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. *Diabetes Care* 1993; **16:** 434–444.

25 Adler AI, Stratton IM, Neil HAW, Yudkin JS, Matthews DR, Cull CA *et al*. Association of systolic blood pressure with macrovascular and microvascular complications of type 2 diabetes (UKPDS 36): prospective observational study. *BMJ* 2000; **321:** 412–419.