Original Article

What is hypertension in chronic haemodialysis? The role of interdialytic blood pressure monitoring

Sandip Mitra, Shahid M. Chandna and Ken Farrington
Renal Unit, Lister Hospital, Stevenage, UK

Abstract

Background. Hypertension in chronic haemodialysis patients contributes significantly to morbidity and mortality. Treatment decisions are usually based on predialysis readings, which may not accurately reflect control during the interdialytic period. Methods. We studied 40 randomly selected subjects on haemodialysis and compared readings by different methods at set times during the dialysis session with the 48-h interdialytic ambulatory readings. Conventional sphygmomanometer, automated Dinamap and Tm 2421(A&D) ambulatory monitor were used for BP measurements.

Results. Conventional sphygmomanometry and self measured automatic readings (Dinamap) were highly correlated (systolic \( r = 0.93, \ P < 0.001 \); diastolic \( r = 0.90, \ P < 0.001 \)). Mean blood pressure on arrival (\( \text{PreC}_0 \)) 158 mmHg systolic, 80 mmHg diastolic and 106 mmHg mean) significantly overestimated the mean ambulatory reading during the 6 h prior to attendance (\( \text{preAm}_{6h} \)) systolic 147 (\( P < 0.01 \)), diastolic 75 (\( P < 0.01 \)), mean 99 (\( P < 0.01 \)). Fifteen patients (41%) demonstrated a marked difference (>20/10 mmHg) between the \( \text{PreC}_0 \) and \( \text{preAm}_{6h} \) (white-coat effect) persisting in seven patients (19%) after a period of rest 10 min predialysis (\( \text{preC}_{10} \)) and present even in self-recorded Dinamap readings. There was a significant negative relationship between the systolic rise and the number of months on dialysis (\( P < 0.05 \)). Mean ambulatory BP on interdialytic day 2 was significantly greater than on day 1 whereas the awake—sleep differences were less on day 2 than day 1, both perhaps reflecting differences in volume status. The 20 min post-dialysis measurement (\( \text{PoC}_{20} \)) for systolic, diastolic, and mean, unlike predialysis (\( \text{PreC}_0 \) and \( \text{preC}_{10} \)), onset (onC) and end of dialysis readings (enC) did not differ significantly from 48 h interdialytic means.

Conclusions. The best representation of interdialytic pressure was the 20-min post-dialysis reading. Walk-in predialysis pressures overestimate mean interdialytic pressures due to a high incidence of white-coat effect, which shows some habituation with time on dialysis. Ambulatory monitoring has a role in evaluating persistent poor blood pressure control in haemodialysis patients.

Key words: ambulatory monitoring; blood pressure; best representative blood pressure; haemodialysis; measurement; white-coat effect

Introduction

Hypertension in chronic haemodialysis (HD) patients contributes significantly to their morbidity and mortality. Epidemiological studies have consistently shown that although treated, blood pressure (BP) frequently remains inadequately controlled in a high proportion of HD patients [1,2]. This is complicated by the high morbidity of both over- and undertreatment [3,4] and by factors peculiar to the HD situation itself. It is difficult to define hypertension in dialysis. Which blood pressure reading should be taken to signify hypertension is more pertinent in dialysed individuals than in the general population because of their fluctuating fluid status and other factors associated with the dialysis session. In the general hypertensive population it is known that the use of single readings as a reliable indicator of the overall BP control is fraught with difficulty because of transient and persistent elevations of pressure in the clinical setting [5]. The variability of casual readings in relation to the dialysis cycle confound management decisions and pose a dilemma with regard to the optimum timing and method of measurement of BP in this setting. Treatment decisions are mostly based on predialysis readings. However the relevance of these readings has been questioned and studies have shown their tendency to overestimate true BP [6]. Epidemiological studies also suggest ambulatory BP control may be a better predictor of target organ damage [7]. We therefore investigated 40 randomly selected patients undergoing haemodialysis without any alteration in medication or dialysis schedule with the aim of comparing methods of measurement.
and comparing casual readings during the dialysis session with 48 h interdialytic ambulatory readings.

**Subjects and methods**

**Patients**

Forty randomly selected stable chronic stable HD patients attending our unit were studied. The patient characteristics of the study group are shown in Table 1. All patients received high-flux bicarbonate dialysis three times per week using biocompatible polysulphone or polyacrylonitrile membranes. Dialysis was prescribed according to a urea kinetic model [8] with mean dialysis duration 160 ± 43 min. The study cohort represented the average haemodialysis population in the centre with respect to age, sex, dialysis duration, and blood pressure control. They achieved their dry weight without symptomatic hypotension or cramps and had acceptable stable interdialytic weight gains. Sixteen patients dialysed in the morning (1030–1200 h) and 24 patients in the afternoon (1230–1600 h). Nine (22%) were on no antihypertensive medications, 55% were on mono- or dual therapy. Drugs used were ACE inhibitors (22 patients), calcium antagonists (14 patients) and beta blockers (3 patients). Antihypertensive medications were not withheld on the day of dialysis and usually taken in the morning. Patients excluded were: (i) those on twice-weekly HD; (ii) those in atrial fibrillation; (iii) those who had undergone hospital admission within the previous month; (iv) those in whom antihypertensive agents had been altered within the previous 2 weeks; and (v) those on early morning or evening dialysis shifts. Four patients had taken off their ambulatory monitor a few hours before arriving in the unit and the results were not used in analysing the white-coat effect.

**Methods**

**Blood pressure measurements**

Mercury column sphygmomanometry was used for manual reading by a trained clinician, taken in a seated position using the phase 5 diastolic and a mean of two repeated measurements. The patient also recorded his/her own BP in the unit using an automated self-measurement Dinamap (Critikon) [9], which downloaded the results directly into a software programme, blinded to the observer. Patients were well acquainted with the recording procedure, as it is a routine protocol in the unit prior to each dialysis. All casual measurements were taken in the seated position with the arm resting and a cuff size suitable for the arm circumference attached to the non-fistula-bearing upper arm.

Ambulatory monitoring was carried out using the Tm2421 A&D Engineering, Milpitas, CA blood pressure monitor. This has been validated and used for clinical and research purposes [10]. BP was measured using cuff size comparable to the seated BP measurements on the non-fistula-bearing arm by a dual microphone system. This system used oscillometric (O) and Korotkoff (K) methods programmed to record BP every 30 min daytime and hourly at night-time (2200–0700 hours). Recorded data was retrieved, processed, and reported using a computer software programme; 74.6% K readings and 95% O readings were successful. Accordingly, the O method readings were used for the main analysis.

**Definitions used**

**Conceptual average BP** Mean predialysis BP from last 10 visits for HD as recorded on the database.

**Systolic load** % of all ambulatory readings > 140 mmHg [11]

**Diastolic load** % of all ambulatory readings > 90 mmHg [11]

**Dippers** > 10% fall in the mean pressure during the night (2200–0700) compared to daytime readings [12]

**Awake–sleep difference** Difference of mean day and night-time BP in the 48-h period.

**Average BP ( AvC )** Mean of pre (PreC0) and post (PoC0) readings.

**Hypertension (casual reading)**

- Systolic > 150 or diastolic > 90 mmHg
- Systolic > 135 or diastolic > 85 mmHg [13]
- Systolic > 140 or diastolic > 90 mmHg [13]

That showing the minimal difference from the mean during the interdialytic period [11]

**White-coat effect** Rise in BP of > 20/10 mmHg in the reading on attendance to the unit above the daytime ambulatory BP during the 6 hs prior to attending the unit.

**Protocol**

BP on arrival for dialysis (PreC0) was checked by the patients themselves using the Dinamap and then by a clinician using sphygmomanometer. The patient then rested in a quiet room for 10 min, after which BP measurement was repeated (PreC10) in a similar manner (by the patient using a Dinamap and by the clinician using sphygmomanometer). An ambulat-

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**Table 1. Patient characteristics at the time of enrolment into the study**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>61.5</td>
<td>(14.8)</td>
<td>21–81</td>
</tr>
<tr>
<td>Months on HD</td>
<td>27</td>
<td>(18.7)</td>
<td>6–78</td>
</tr>
<tr>
<td>IDWG (kg)</td>
<td>1.34</td>
<td>(0.72)</td>
<td>0.4–3.7</td>
</tr>
<tr>
<td>AH drugs</td>
<td>1.5</td>
<td>(1.0)</td>
<td>0–4</td>
</tr>
<tr>
<td>Epo (IU/week)</td>
<td>6000</td>
<td>(4600)</td>
<td>0–20000</td>
</tr>
<tr>
<td>Kt/V</td>
<td>1.7</td>
<td>(1.73)</td>
<td>0–4.8</td>
</tr>
<tr>
<td>Ultrafiltration (l/h)</td>
<td>0.59</td>
<td>(0.26)</td>
<td>0.19–1.2</td>
</tr>
<tr>
<td>Sex m:f</td>
<td>35:5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetic</td>
<td>10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Kt/V, mean of delivered Kt/V measurements performed within the 4 months prior to the study; KRU, residual renal function as urea clearances (ml/min); AH drugs, no. of antihypertensive medications; Epo, erythropoietin dosage; IDWG, interdialytic weight gain (kg); SD, standard deviation.
Conclusion

The results of this study highlight the importance of understanding the differences between casual and ambulatory BP measurements. The significant overestimation of casual BP readings compared to ambulatory monitoring underscores the limitations of using casual readings alone, especially in hypertensive patients. The development of algorithms that take into account patient characteristics or the use of more accurate devices could help improve the accuracy of BP measurements. Further research is needed to explore the long-term implications of these findings on cardiovascular health and to evaluate the clinical significance of the variations observed.

Acknowledgments

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References

Fig. 1. Bland–Altman analysis of sphygmomanometer and Dinamap (a) systolic and (b) diastolic readings. Reference lines indicate the mean difference of the two methods and their limits of agreement (± 2 SE from the mean differences).

Fig. 2. Error bars showing mean differences of BP during dialysis from the average 48-h ambulatory pressures and variability for (a) systolic and (b) mean BP (limits indicate 95% confidence intervals). *P > 0.05 (no significant difference from the 48-h average) Con av, conceptual average BP. For key to abbreviations, refer to footnote of Table 3.

Table 3. Blood pressure measurements during dialysis cycle compared with interdialytic pressures

<table>
<thead>
<tr>
<th></th>
<th>Systolic</th>
<th>Diastolic</th>
<th>MBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>48-h average</td>
<td>140 (21.5)</td>
<td>71 (11)</td>
<td>94 (13)</td>
</tr>
<tr>
<td>Conceptual</td>
<td>157 (22)</td>
<td>78 (10)</td>
<td>104 (12)</td>
</tr>
<tr>
<td>Average</td>
<td>150 (21)</td>
<td>74 (10)</td>
<td>99 (12)</td>
</tr>
<tr>
<td>PreC</td>
<td>158 (20)</td>
<td>80 (11)</td>
<td>106 (12)</td>
</tr>
<tr>
<td>PreC&lt;sub&gt;10&lt;/sub&gt;</td>
<td>150 (21)</td>
<td>74 (10)</td>
<td>99 (12)</td>
</tr>
<tr>
<td>OnC</td>
<td>146 (23)</td>
<td>76 (16)</td>
<td>99 (15)</td>
</tr>
<tr>
<td>EnC</td>
<td>124 (31)</td>
<td>70 (13)*</td>
<td>88 (16)</td>
</tr>
<tr>
<td>PoC&lt;sub&gt;20&lt;/sub&gt;</td>
<td>136 (25)*</td>
<td>70 (11)*</td>
<td>92 (14)*</td>
</tr>
<tr>
<td>AvC</td>
<td>144 (21)</td>
<td>74 (10)</td>
<td>97 (12)</td>
</tr>
</tbody>
</table>

* P = n.s. (no sign. difference from the 48-h mean). Student’s t-test paired with 48-h readings for systolic, diastolic, and mean. Values rounded to the nearest integer. PreC, predialysis BP on arrival; PreC<sub>10</sub>, 10 min predialysis BP; OnC, onset of dialysis BP; EnC, BP end of dialysis; PoC<sub>20</sub>, 20 min post-dialysis BP; AvC, average of pre and post-dialysis BP; MBP, mean blood pressure.

**Relationship to interdialytic fluid gains**

We could not demonstrate a significant relationship of weight gain or ultrafiltration volume with casual BP on dialysis, white-coat effect or nocturnal dipping except for a weak but significant correlation between the BP at the end of dialysis (EnC) and ultrafiltration volume (P < 0.05; r = −0.40). During the interdialytic period, however, average ambulatory BP on day 2 was higher than on day 1 (systolic 147 vs 139 mm P < 0.05; diastolic 74 vs 71 mm P = n.s.). The awake—sleep difference was significantly reduced on day 2 compared with day 1 (1.6 vs 7.5 mmHg systolic; P < 0.05).
What is hypertension in chronic haemodialysis?

**Discussion**

The measurement of BP for clinical evaluation of the HD patient may be subject to three types of error. First is the error due to the measurement procedure itself. We confirmed that same arm BP measurements by Dinamap and the clinician are comparable though not necessarily identical [17]. The agreement between mercury column and Dinamap determinations were within 10 mmHg in 90% systolic and 98% of diastolic readings. The error between two devices may be due to (i) consecutive rather than simultaneous readings, or (ii) systematic differences, which can be corrected for by adjusting for the average difference (negligible in this study) between the devices. The overall level of agreement is reassuring and suggests that either may be used with confidence in the clinical setting.

The second type of error arises from the spurious elevation of BP in the clinical setting often attributed to an emotional reaction to the involvement of a clinician. The ‘white-coat effect’ is defined as transient rise in BP that occurs in the clinical setting [18]. We observed this phenomenon in almost 40% of arrival Conceptual average systolic pressures, which improved to 19% after a period of rest. The effect did not persist throughout the dialysis session. The timing of the dialysis session did not influence the presence of WCE. There seemed to be no noticeable difference when the physician took the BP. The involvement of the physician does not seem to be a determining factor in the white-coat effect. This study confirms that the white-coat effect persists even in patients on antihypertensive therapy [19]. The negative relationship with duration on dialysis could be due to habituation to clinic measurements with time or due to the longer duration of antihypertensive therapy.

There is little data on the white-coat phenomenon in the dialysis population, though in a study on 13 normotensive HD patients [20] large differences were noted between the predialysis readings and interval pressures just before dialysis. The timing of the predialysis blood pressure measurement is therefore crucial. The initial arousal response can be minimized using readings after a rest period. The mechanisms and prognostic significance of the white-coat effect are not fully understood [14]. The response occurs in about 20% of the general hypertensive population [21],

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**Table 4. Comparison of groups with and without white-coat effect**

<table>
<thead>
<tr>
<th></th>
<th>WCE absent</th>
<th>WCE present</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number</strong></td>
<td>21 patients</td>
<td>15 patients</td>
</tr>
<tr>
<td><strong>Sex (F:M)</strong></td>
<td>2:19</td>
<td>3:12</td>
</tr>
<tr>
<td><strong>Diabetic vs non-diabetic</strong></td>
<td>6:15 (28%)</td>
<td>4:11 (27%)</td>
</tr>
</tbody>
</table>

| Age (years) | 65 | 14 | 58 | 14 |
| No. of anti-hypertensive drugs | 1.5 | 1 | 1.6 | 1 |
| Weekly Epo dose (units) | 5433 | 3166 | 7167 | 3824 |
| Inter-dialytic weight gain (kg) | 1.27 | 0.58 | 1.35 | 0.84 |
| Kt/V | 1.21 | 0.20 | 1.24 | 0.24 |
| Conceptual average systolic BP | 150 | 11 | 176 | 12 |
| Conceptual average diastolic BP* | 73 | 10 | 90 | 14 |
| Average 48-h diastolic BP | 71 | 11 | 72 | 11 |
| Average 48-h mean BP | 95 | 13 | 94 | 11 |
| Average 48-h systolic BP | 141 | 24 | 137 | 18 |
| Pulse (per min) | 72 | 10.7 | 74 | 7.5 |
| 48-h Aw–sl diff (diastolic) | 3.5 | 4.3 | 5.8 | 7.1 |
| 48-h Aw–sl diff (systolic)* | 3.2 | 5.5 | 10.5 | 4.5 |

*Significance of *P* <0.05. WCE, white-coat effect; Aw–sl diff, awake–sleep difference. Key to other abbreviations, please see Table 1 footnote.
is more common in females and blacks and usually disappears on repeated measurements. In the non-dialysis population it is associated with elevated plasma level of various hormones including catecholamines, cortisol, vasopressin, endorphins, and a primary role of the sympathetic system has been suggested [22]. The white-coat phenomenon may be more common in renal patients than in the general hypertensive population [23] perhaps due to an exaggerated sympathetic response conditioned by uraemia. It is noticeable that in the group not demonstrating the white-coat effect WCE(−) there appeared to be a gradual rise in BP before dialyses, whereas in the group demonstrating the effect WCE(+) BP seemed stable in the interdialytic period before an abrupt predialysis rise (Figure 3). Perhaps there is an increased sensitivity to fluid accumulation in the WCE(−) group which may be determined by a sustained sympathetic outflow, whereas the sympathetic surge in the WCE(+) group is more transient. The environment of a busy haemodialysis unit may have a significant influence on the predialysis surge, as may the pressures of travelling to the unit and the fear of needles. Because of the unpredictability of the effect, we recommend that this be carefully considered when assessing resistant predialysis hypertension.

The third error arises from the variability of BP during the dialysis cycle. The large swings in pressure during the dialysis procedure are not fully understood. The overdiagnosis of hypertension using predialysis readings has been observed in many studies [6]. The practice of withholding antihypertensive medication predialysis has been implicated [1] but was not a factor in this study. Even after elimination of the initial arousal phenomenon, predialysis BP poorly reflected interval pressures [6]. The changes in BP during dialysis could reflect volume removal, removal of vasoactive factors, and alterations in arterial compliance and sympathetic activity caused by removal of uraemic toxins. Despite poor correlation of blood pressures on dialysis with weight gains the differences in day 2 and 1 average daytime, night-time BP and awake–sleep differences, suggest some influence of fluid accumulation on diurnal fluctuations of 48 h BP between dialyses.

The 20-min post-dialytic BP (PoC20) appears to be best approximation of the ambulatory interdialytic values in the stable chronic dialysis population. Similar findings have been reported by Kooman et al. [6] while others report unacceptable variability in the predialytic reading [14]. There is significant underestimation of interdialytic means if BP is recorded immediately after dialysis. In our patients the fall in arterial pressure during dialysis recovered rather than dipped post-dialysis though Battle et al. observed a decline in BP in the hour immediately after dialysis [24]. The variation may relate to differences in baseline hydration. The recovery of the 20 min post-dialysis reading may be related to compensatory vascular refilling (fluid rebound) which is maximal in the first half-hour post-ultrafiltration [25]. Allowing this period of equilibration is essential to obtain reliable post-dialysis measurements.

In conclusion, the timing of casual predialysis and post-dialysis BP readings is crucial. Both can be biased by the dialysis procedure itself (white-coat effect in the former and fluid rebound in the latter). The traditional diagnosis of hypertension based solely on predialysis clinic readings can lead to gross overestimation attributable to a white-coat effect. This is an important cause of blood pressure variability and is significant even in self-recorded blood pressure measurements. The best single approximation of interdialytic BP is the 20-min post-dialytic reading. Poor control or sustained hypertension with high clinic BP, despite multiple drug treatment should be assessed by ambulatory monitoring to eliminate overshooting reactions, provide supplemental information about pressure load and variability, and avoid inappropriate treatment. Prospective end-point studies are required to authenticate the relationship between ambulatory BP values and measurements in the dialysis units and the use of both in predicting cardiovascular morbidity and mortality in HD patients.

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