Original Article

Ambulatory blood pressure monitoring and progression in patients with IgA nephropathy

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Abstract

Background. Hypertension is a recognized marker of poor prognosis in IgA nephropathy.

Methods. The present study investigated the prevalence of white-coat hypertension, the diurnal rhythm of blood pressure (BP), the effectiveness of antihypertensive drug therapy, and the effect of the above on the progression of the kidney disease in IgA nephropathy. One hundred twenty-six IgA nephropathy patients were selected consecutively for 24-h ambulatory blood pressure monitoring (ABPM). Fifty-five patients were normotensive and 71 were treated hypertensives. Their antihypertensive drugs were angiotensin-converting enzyme inhibitors (ACEI) alone or in combination with calcium-channel blockers (CCB).

Results. The mean night-time BP of normotensives (108 ± 9/67 ± 6 mmHg) was significantly lower than their day-time BP (125 ± 8/82 ± 7 mmHg, P < 0.05). There was no significant difference between the mean day-time and night-time BP in hypertensive patients (125 ± 9/82 ± 7 mmHg vs 128 ± 10/85 ± 9 mmHg). The circadian variation of BP was preserved ('dippers') in 82% of the normotensive and 7% of the hypertensive patients (P < 0.001). There were 10 ‘white-coat hypertensives’ among the patients classified as normotensives with ABPM (mean office blood pressure 149 ± 7/96 ± 8 mmHg, 24-h blood pressure 127 ± 6/83 ± 5 mmHg, P < 0.05) and 14 among treated hypertensives (mean office BP 152 ± 8/98 ± 6 mmHg, 24-h BP 130 ± 4/85 ± 8 mmHg, P < 0.05). There was no difference in mean day-time BP among normotensive and treated hypertensive patients (125 ± 8/81 ± 5 mmHg vs 128 ± 10/85 ± 9 mmHg). Hypertensives had significantly higher night-time BP (125 ± 9/85 ± 9 mmHg) than normotensives (108 ± 9/67 ± 6 mmHg, P < 0.001). There was no difference in serum creatinine levels among the different groups at the time of the ABPM. However, thirty-six ± 4.1 months after the ABPM, hypertensive patients (n = 52) had higher serum creatinine levels (124 ± 32 μmol/l) than at the time of the ABPM (101 ± 28 μmol/l). The serum creatinine of normotensive patients (n = 43) did not change during the follow-up period. ‘Non-dipper’ normotensives (n = 10) had significantly higher serum creatinine levels at the end of the follow-up period than at its beginning (106 ± 17 μmol/l vs 89 ± 18 μmol/l, P < 0.05). There was no increase in serum creatinine of ‘dipper’ normotensives. The mean serum creatinine of ‘white-coat hypertensives’ was significantly higher at the end of the study period than at its beginning.

Conclusions. There is no diurnal blood pressure variation in most of the hypertensive IgA nephropathy patients. ACEI and CCB treatment have better effect on day-time than night-time hypertension. The lack of the circadian rhythm and ‘white-coat hypertension’ seems to accelerate the progression of IgA nephropathy.

Key words: ambulatory blood pressure monitoring; diurnal blood pressure rhythm; IgA nephropathy; progression of renal disease; white-coat hypertension

Introduction

Primary IgA nephropathy is the most common type of glomerulonephritis worldwide with differences in prevalence in the various geographical areas [1,2]. During the follow-up chronic renal failure develops frequently [3,4]. The curves of renal survival from numerous series of patients that have been followed up have shown 5–15% of patients with end-stage renal disease after 5 years from the apparent onset of the disease, 10–20% after 10 years, 15–30% after 15 years, and 20–50% after 20 years [2].

The kidney and high blood pressure are closely related. Renal vascular damage caused by arterial hypertension participates in alterations of the systemic vascular function and structure [5]. It has been hypothesized that in essential hypertension, the increase in blood pressure is needed to maintain glomerular filtration rate and sodium excretion within normal limits. Renal vasoconstriction seems to be functional in the
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initial stages of the disease and can be reversed with the administration of drugs such as CCBs and ACEIs. Renal vasoconstriction remains constant thereafter as a consequence of the nephrosclerosis that is secondary to persistently elevated blood pressure [6]. The other way around, hypertension can accelerate the decline of renal function in kidney diseases. The incidence of systemic hypertension in patients with IgA nephropathy after a short mean follow-up (2–4 years) was 12% in North America, 31.7% in Europe, and 15.5% in the Asian–Pacific area [2]. Hypertension is a recognized marker of poor prognosis in IgA nephropathy; renal survival rate of hypertensive patients is lower than that of non-hypertensive patients [1,3,4,7–9].

The increasing availability of ambulatory blood pressure monitoring (ABPM) has shifted interest in blood pressure measurement from the doctor’s office to the entire 24-h period. The use of ABPM has allowed diagnosis of ‘white-coat hypertension’, in which blood pressures are higher on office measurements than on ambulatory monitoring. It can be utilized to identify ‘dippers’ and ‘non-dippers’ among patients [10–12]. Routine office blood pressure recordings correlate poorly with left ventricular mass, a sign of early target organ damage. At the same time, ambulatory blood pressure shows good correlation with left ventricular mass [13–15].

The aim of the present study was to investigate the prevalence of ‘white-coat hypertension’, the diurnal rhythm of blood pressure and the effectiveness of antihypertensive drug therapy in IgA nephropathy patients. We have also investigated the effect of ‘white-coat hypertension’, lost or preserved diurnal blood pressure variation and treatment of hypertension on the progression of IgA nephropathy.

Subjects and methods

One hundred twenty-six non-uremic patients with IgA nephropathy confirmed by renal biopsy were selected consecutively. Fifty-five patients (36 male, 19 female) were normotensive; age 37.7 ± 10 years (mean ± SD). Normotension and hypertension was defined according to the WHO criteria. Seventy-one patients (57 male, 14 female) were hypertensive; age 46.4 ± 12 years (mean ± SD). ABPM was carried out using an automatic device (Meditech ABPM-02, Meditech Kft., Hungary) based on the cuff-oscilometric method. The blood pressure was monitored for 24 h using the above-described device. ABPM readings were taken on the patients non-dominant arm every 15 min around the clock day-time (from 06.00 to 22.00 hours) and every 20 min night-time (from 22.00 to 06.00 hours). Office blood pressures are expressed as mean values of at least three casual measurements taken at different visits in sitting position in standardized fashion using appropriately sized cuffs and a random-zero mercury sphygmomanometer on the non-dominant arm. After the ABPM the patients were followed prospectively.

Hypertensive patients (n = 71) were mild or borderline hypertensives according to the WHO criteria, treated with ACEI in monotherapy (n = 43) or in combination with CCB agents (n = 28).

The cutoff points for clinic and ambulatory blood pressure used to define ‘white-coat hypertension’ were the following: clinic blood pressure over 140/90 mmHg; 24-h mean ambulatory blood pressure less than 135/85 mmHg [11]. Clinic blood pressures considered were averages of at least three readings taken at different visits according to the WHO criteria.

‘Dippers’ were classified as patients having mean night-time systolic blood pressure reduction of at least 10% compared to the corresponding day-time values; ‘non-dippers’ were classified as those, whose night-time blood pressure did not drop or was not reduced by at least 10% [1,15,16]. Ninety-five patients have been followed up for 36 ± 4.1 months. At the time of the ABPM and at the end of the follow-up period serum creatinine levels of the different groups (‘dipper’ and ‘non-dipper’) were measured and compared.

Variables of interest were described in terms of their means and standard deviation. Statistical evaluations were performed by Student’s t test.

Results

Diurnal blood pressure variation

Normotensive IgA nephropathy patients (n = 55) had significantly higher day-time than night-time systolic and diastolic blood pressure. In treated hypertensive IgA nephropathy patients (n = 71) the mean day-time systolic and diastolic blood pressure did not differ from the mean night-time blood pressures (Figure 1).

Eighty-two per cent of the normotensive patients were ‘dippers’. Ninety-three per cent of the hypertensives according to the WHO criteria, treated with ACEI in monotherapy (n = 43) or with CCB agents (n = 28). We have also observed the ‘white-coat effect’ in 14 treated hypertensives, too (mean office blood pressure 152 ± 8/98 ± 6 mmHg, mean 24-h blood pressure 130 ± 4/85 ± 8 mmHg, P < 0.05, Table 1).

Effectiveness of antihypertensive therapy

The mean day-time blood pressure of normotensive and treated hypertensive IgA nephropathy patients was not different. Normotensives had significantly lower night-time and 24-h blood pressure, than treated hypertensives (Figure 1).

Progression and blood pressure

The serum creatinine of 43 normotensive (age 38.6 ± 10 years) and 52 hypertensive patients (age 47.2 ± 12 years) has been compared at the time of the ABPM and 36 ± 4.1 months following the ABPM. Thirty-six months after the ABPM treated hypertensives had significantly higher serum creatinine than at the time
Fig. 1. Blood pressure of normotensive and hypertensive IgANP patients \((n=126)\). NT, normotensive patients; HT, treated hypertensive patients; sys, systolic blood pressure; dia, diastolic blood pressure.

Table 1. ‘White-coat effect’ in normotensive and treated hypertensive IgANP patients \((n=24)\)

<table>
<thead>
<tr>
<th></th>
<th>Office blood pressure</th>
<th>(P)</th>
<th>Mean 24-h blood pressure (ABPM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>((\text{mmHg, mean} \pm \text{SD}))</td>
<td></td>
<td>((\text{mmHg, mean} \pm \text{SD}))</td>
</tr>
<tr>
<td>Normotensive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>((n=55))</td>
<td>10</td>
<td>149 \pm 7/96 \pm 8</td>
<td>(P&lt;0.05)</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>14</td>
<td>152 \pm 8/98 \pm 6</td>
<td>(P&lt;0.05)</td>
</tr>
</tbody>
</table>

of the ABPM \((P<0.05)\). The serum creatinine of normotensive patients was not higher at the end of the follow-up period than at the time of the ABPM (Table 2). There was no difference in mean body weight and male/female ratio between the groups (data not shown). Thirty-six \(\pm 4.1\) months after the ABPM, the serum creatinine of ‘dipper’ normotensives was not higher than at the time of the ABPM. The serum creatinine of ‘non-dipper’ normotensives was significantly higher at the end of the follow-up period than at the time of the ABPM \((P<0.05, \text{Table 2})\). There was no difference in mean body weight and male/female ratio between ‘dippers’ and ‘non-dippers’ (data not shown). The mean serum creatinine of ‘white-coat hypertensives’ \((n=10)\) was not different from that of other (‘real’) normotensives \((n=33)\) at the beginning of the 36-months follow-up period, but it was significantly higher at the end of it. The serum creatinine of ‘real’ normotensive patients did not change during the follow-up period (Table 2).

There was no significant difference in urinary protein

Table 2. Serum creatinine of IgA nephropathy patients at the beginning and at the end of the follow-up period

<table>
<thead>
<tr>
<th></th>
<th>Serum creatinine at the time of the ABPM ((\mu\text{mol/l, mean} \pm \text{SD}))</th>
<th>(P)</th>
<th>Serum creatinine 36 (\pm 4.1) month after the ABPM ((\mu\text{mol/l, mean} \pm \text{SD}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotensives ((n=43))</td>
<td>89 \pm 17</td>
<td>n.s.</td>
<td>93 \pm 22</td>
</tr>
<tr>
<td>Hypertensives ((n=52))</td>
<td>101 \pm 28</td>
<td>(P&lt;0.05)</td>
<td>124 \pm 32</td>
</tr>
<tr>
<td>‘Dipper’ normotensives ((n=28))</td>
<td>81 \pm 14</td>
<td>n.s.</td>
<td>84 \pm 18</td>
</tr>
<tr>
<td>‘Non-dipper’ normotensives ((n=8))</td>
<td>89 \pm 18</td>
<td>(P&lt;0.05)</td>
<td>106 \pm 17</td>
</tr>
<tr>
<td>‘Real’ normotensives ((n=33))</td>
<td>90 \pm 16</td>
<td>n.s.</td>
<td>89 \pm 22</td>
</tr>
<tr>
<td>‘White coat hypertensives’ ((n=10))</td>
<td>88 \pm 19</td>
<td>(P&lt;0.05)</td>
<td>105 \pm 19</td>
</tr>
</tbody>
</table>
excretion at the time of ABPM between normotensive (0.68 ± 0.42 g/day) and hypertensive patients (0.79 ± 0.56 g/day). Six from the 55 normotensive and 11 from the 71 hypertensive patients had urinary protein excretion of more than 1.5 g/day.

Discussion

As casually measured high blood pressure seems to accelerate the decline of renal function in IgA nephropathy [7,9,17,18], it is of interest to study the 24-h blood pressure of normotensive and hypertensive IgA nephropathy patients and to analyse the different parameters of ambulatory blood pressure measurements. With the increasing availability of ABPM it became possible not only to measure the blood pressure during 24 h, but also to identify between ‘dippers’ and ‘non-dippers’, ‘white-coat hypertensives’ and ‘real’ hypertensives and to control better the treatment of high blood pressure during day- and night-time. In early IgA nephropathy ambulatory blood pressure is already slightly elevated and diastolic left ventricular malfunction can be detected [19].

According to our results, most of normotensive IgA nephropathy patients have normal diurnal blood pressure variation. As in histologically not specified chronic glomerulonephritic patients and in other types of secondary hypertension [20], in hypertensive IgA nephropathy patients the diurnal blood pressure rhythm has disappeared. Eighty-two per cent of the normotensive IgA nephropathy patients were classified as ‘dippers’, which is similar to the percentage of ‘dippers’ in the normotensive population with no kidney disease. Ninety-three per cent of hypertensive IgA nephropathy patients were classified as ‘non-dippers’, with no decrease or, even, some increase in nocturnal blood pressure.

‘White-coat hypertension’ has been described in mild forms of essential hypertension [12]. We observed the same phenomenon in 18% of our normotensive IgA nephropathy patients, which is very similar to the prevalence of ‘white-coat hypertension’ in patients with mild essential hypertension. Furthermore, we observed the ‘white-coat phenomenon’ in 20% of our treated hypertensive IgA nephropathy patients, too. If we do not count on this phenomenon, we may treat normotensive patients with antihypertensive drugs with no purpose or we may overtreat hypertensive patients. Such treatment is not innocuous, it may cause hypertension and hypoperfusion of the glomerulonephritic kidney, which may accelerate the decline of renal function. Antihypertensive drugs are expensive and labelling patients as hypertensive might be a psychic burden to them.

Treated hypertensive and normotensive IgA nephropathy patients had similar day-time blood pressure values, but the night-time blood pressure was decreased in normotensives and unchanged in hypertensives. It means that hypertensives had higher than normal night-time blood pressure and mean 24-h blood pressure. This may explain the faster deterioration of renal function in these treated hypertensive patients.

The progression of the kidney disease seemed to be faster in ‘non-dipper’ than in ‘dipper’ normotensive IgA nephropathy patients, too. This underlines the importance of the night-time blood pressure in the development of target organ damage. The higher blood pressure load caused by higher nigh-time blood pressure [21] seems to be important in the decline of renal function in both hypertensive and normotensive IgA nephropathy patients.

The progression of the kidney disease was faster in ‘white-coat hypertensive’ patients than in ‘real’ normotensive patients. It has been shown that office hypertension is not an innocent blood pressure variant in essential hypertension [22]. This seems to be the case in IgA nephropathy, too. The decline of renal function in these patients seems to be faster, and most of these patients may develop hypertension later on.

According to our results, the lack of the blood pressure ‘dip’ at night seems to accelerate the decrease in renal function in IgA nephropathy patients. Early antihypertensive therapy providing adequate 24-h blood pressure control—eventually even mimicking the normal nocturnal decrease of blood pressure—may slow down the development of end-stage renal failure in these patients. ACEI and CCB treatment seems to be not effective to resettle the diurnal blood pressure variation. The percentage of ‘white-coat hypertensives’ among normotensive IgA nephropathy patients and mild hypertensives with normal or nearly normal renal function is similar and it may accelerate the progression of the kidney disease.

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