Inappropriate opinion on normal blood pressure and impact on compliance in chronic hemodialysis

Abstract

Background: Arterial hypertension (AH) associated with cardiovascular disease is often responsible for morbidity and mortality in chronic hemodialysed patients (CHD). Noncompliance with antihypertensives could be related to distorted view on normal blood pressure (NBP).

Purpose: To examine if CHD patients consider increased blood pressure (BP) for normal and consequently have poor compliance with antihypertensive therapy.

Patients and Methods: 202 CHD patients (aged 25–85 years) at University Hospital Centre Osijek, Croatia, completed a questionnaire on maximal NBP, compliance to antihypertensives and symptoms related to BP variations. Data on medical history and AH control were obtained from their medical records. Optimal BP before hemodialysis (HD) session was considered <140/90 mmHg, mean arterial pressure (MAP) <107 mmHg, corresponding to the high normal BP according to guidelines ESH-ESC 2007.

Result: 57% of 202 patients declared maximum acceptable systolic BP >139 mmHg (median 150, range 140–180). Majority of them would not take antihypertensives and reported symptoms occurring by BP lower than preferred. The year of AH diagnosis differed significantly from the initial year of antihypertensive therapy (P<0.001), indicating delayed treatment. Patients with distorted view on NBP were older (P=0.012), took more antihypertensives (P=0.043) and had higher predialysis MAP (P=0.019) in comparison with other patients.

Conclusion: CHD patients consider NBP to be higher than officially recommended. Majority had poorly regulated AH due to noncompliance with antihypertensives therapy. Different view on NBP could be attributed to their symptoms occurring by BP lower than preferred. They seem to be adapted to increased BP. The question remains whether this is a consequence of delayed AH treatment or inadequate guidelines for CHD patients.

INTRODUCTION

Arterial hypertension (AH) is common among chronic hemodialysed patients. Hypertension is observed in approximately 80% to 90% of patients by the time chronic kidney disease (CKD) progresses to end-stage renal failure (1). Cardiovascular diseases (CVD) remain the leading cause of death among patients on dialysis and after renal transplantation (2). According to Collins et al., 45% of all deaths of hemodialysed patients can be attributed to cardiovascular causes (3). Still
there are no specific guidelines for this population of patients. According to the current literature and guidelines (National Kidney Foundation Task Forces on Cardiovascular Disease), blood pressure (BP) is recommended to be lower than 140/90 mmHg in hypertensive patients on renal replacement therapy (4). The prevalence of AH in general population is higher than it was several decades ago, and in Europe it is approximately 40%. According to the results of the epidemiology of AH in Croatia study (EH-UH), the prevalence of AH in Croatia is 37.5% (5). Women are more aware of the disorder, they were treated more often, and BP control was more frequently achieved than in men. The prevalence of CKD in stage 3–5 (glomerular filtration rate <60 mL/min/1.73 m²) in general population was 4.7%, but considering also those suffering from hypertension, diabetes and those older than 55 years the prevalence of CKD could be up to 93.2% (6). The most common pattern of BP in dialysis patients is systolic hypertension associated with a wide pulse pressure due to atherosclerotic arterial stiffness (7, 8). Insufficient volume removal is often the major factor responsible for dysreflexia-refractory hypertension (9, 10). Both fluid overload and dehydration are linked to an increased morbidity in hemodialysed patients (11). Volume depletion during hemodialysis (HD) session can cause intradialytic hypotension. It is associated with appearance of symptoms, which makes treatment unpleasant and indirectly affects the prescribed treatment and patients’ adherence to taking antihypertensive treatment before HD session (12). Several additional factors also contribute to increase in sympathetic outflow in this population including renal ischemia, increased activity of the renin–angiotensin system, nocturnal hypoxemia and prevalent co-morbidities such as chronic heart failure (13, 14, 15). Renal ischemia is probably an important primary event leading to increased sympathetic nervous system activity. Enhanced sympathetic nervous system activity appears to be a direct effect of primary NO deficiency and plays an important role in the genesis of hypertension in NO deficiency. NO synthetase activity progressively decreases in chronic renal failure, which results in unbalanced NO and angiotensin activity. Chronic NO deficiency induced intraglomerular platelet aggregation and glomerular injury, which was ameliorated by renal denervation. Progression of renal insufficiency could be reduced by using α1-adrenoceptor blocker or the ACE inhibitor. Observational studies in HD patients have yielded paradoxical results on the relationship between BP level and cardiovascular morbidity and mortality risk. These relationships may be different from those observed in general population (16). Although increased BP is associated with adverse outcomes in general population, elevated BP is associated with decreased mortality in patients with end-stage renal disease undergoing maintenance HD (17). Low BP appears to be associated with higher mortality during the early years of dialysis, whereas high BP is associated with mortality in long-term follow-up. Increased mortality risk associated with lower BP indicates the presence of heart failure and inability to increase BP level (18).

Arterial hypertension is more common in both type 1 and type 2 diabetes mellitus than in general population (19). Kidney disease is almost always the source of hypertension in type 1 diabetes. In type 2 diabetes, many people who have hypertension, impaired glucose tolerance and other features of metabolic syndrome will eventually develop diabetes mellitus. Hypervolemia in diabetes can be partially explained by active reabsorption of glucose and ketones in the kidney as sodium salts, abnormalities in several sodium- and volume-regulating systems, such as the renin–angiotensin-aldosterone system, insulin, atrial natriuretic peptide, sodium transport pathways, intrarenal dopamine production, vessel compliance, and renal function, resulting in an enhanced propensity to hypertension (20). It is recommended that diabetic patients should be treated with antihypertensives if BP is ≥130/80 mmHg (21). People with type 2 diabetes have a greater incidence of cardiovascular disease, cerebrovascular disease and renal disease than the general population. Each 10 mmHg reduction in systolic BP was associated with a 12% decrease in the risk of any end point related to diabetes and a 15% reduction in the risk of death related to diabetes (22). In the Atherosclerosis Risk in Communities (ARIC) study, individuals with systolic BP (SBP)/diastolic BP (DBP) >140/90 mmHg were 2.5 times more likely to develop diabetes than their normotensive counterparts (23, 41).

Observational studies and their meta-analysis have shown that late referral of patients with CKD to nephrologists is associated with poor clinical outcomes (21, 24). The National Kidney Foundation-Kidney Disease Outcomes Quality Initiatives (K-DOQI) guidelines recommend the patients with CKD to be referred to nephrologists when glomerular filtration rate (GFR) falls below 30 mL/min (Stage 4 CKD), and earlier if possible (25). Despite the existence of these guidelines, nearly 15–80% of patients who start dialysis are referred late (26). Noncompliant behavior is likely one of the most common causes of treatment failure for chronic conditions (27). Lack of symptoms in hypertension together with a low tolerability of some antihypertensive drugs are some of the most common reasons for patients to discontinue treatment or not take the medication as prescribed.

We have frequently encountered chronic HD patients avoiding prescribed antihypertensive medication. We examined the hypothesis that chronic HD patients have increased BP values for normal and that their poor BP control is partly related to consecutive noncompliance with antihypertensive medication.

**PATIENTS AND METHODS**

The study included all 202 chronic hemodialysed patients (University Hospital Centre Osijek, Osijek, Croatia), ranging in age from 25 to 85 years (mean 64 ± 13 years, 103 males). The study was conducted in 2010. All patients provided informed consent for participation in the study. 24 patients were undergoing HD two times and 178 patients three times per week, using dialyzers
with bicarbonate buffer and polysulfone membranes. The study was conducted using a questionnaire and by taking data from medical records. Current arterial BP control data were updated from their HD records. The questionnaire was completed during a regular dialysis session. The questionnaire consisted of several types of questions: some referred to the patients’ general characteristics (age, gender, education); other questions were related to the patients’ opinion on which factors could have influenced BP variations, e.g. smoking, fat food, salt, obesity and physical activity. Other questions were related to their compliance to the treatment regimen: if they were taking antihypertensives regularly, before HD session, depending on BP variations, which antihypertensives were currently prescribed, about their knowledge about medicines for AH. Several questions were related to the patient’s history of the disease: duration of AH, treatment of AH and dialysis duration. Table 1 and Table 2 show the questions addressed to patients. BP was measured with mercury column sphygmomanometer on the opposite arm of vascular access in a recumbent subject before, during and after HD session by a nurse as regular procedure in monitoring patients during a HD session. Disappearance of bruits (Korotkoff phase V) identified diastolic BP. Means of the BP values during three consecutive hemodialysis sessions were taken from their recent medical records. Mean arterial pressure (MAP) was measured according to the formula: MAP = (systolic BP + 2 × diastolic BP)/3. Categories of BP values were compared to those recommended by the guidelines (National Kidney Foundation Task Forces on Cardiovascular Disease ESH-ESC 2007). We also took the data on diabetes, antihypertensive medication and underlying renal disease from medical records. Regarding the patients’ perception of BP values, we divided the subjects into the two groups: the patients who considered maximum normal systolic BP lower than 140 mmHg (Subgroup 1) and the patients who considered maximum

**TABLE 1**

Demographics of the chronic hemodialysed patients (N=202).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All patients (N=202)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>64±13</td>
</tr>
<tr>
<td></td>
<td>range 25–85</td>
</tr>
<tr>
<td>Gender males:females</td>
<td>103:99</td>
</tr>
</tbody>
</table>

<sup>1</sup>Statistical significance in age (years) between the subgroups; t=–2.546, P=0.012. There is no statistical difference in other patients’ characteristics.

**TABLE 2**

Answers to questions on arterial hypertension.

<table>
<thead>
<tr>
<th>Question</th>
<th>Frequency (% of the answers)&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All patients (N=202)</td>
</tr>
<tr>
<td>Taking antihypertensive treatment regularly (n, %)</td>
<td>123 (71.9%)</td>
</tr>
<tr>
<td>Currently prescribed antihypertensive (n, %)</td>
<td>132 (77.2%)</td>
</tr>
<tr>
<td>Knowledge about medicines for AH (n, %)</td>
<td>34 (16.8%)</td>
</tr>
<tr>
<td>Taking antihypertensive treatment before hemodialysis session (n, %)</td>
<td>107 (63.5%)</td>
</tr>
<tr>
<td>Taking antihypertensives depending on BP variations (n, %)</td>
<td>111 (64.9%)</td>
</tr>
<tr>
<td>Impact of obesity on BP values (n, %)</td>
<td>122 (75.3%)</td>
</tr>
<tr>
<td>Impact of salt on BP values (n, %)</td>
<td>164 (89.6%)</td>
</tr>
<tr>
<td>Impact of fat food on BP values (n, %)</td>
<td>147 (82.1%)</td>
</tr>
<tr>
<td>Impact of smoking on BP values (n, %)</td>
<td>122 (74.4%)</td>
</tr>
<tr>
<td>Impact of physical activity on BP values (n, %)</td>
<td>128 (73.6%)</td>
</tr>
<tr>
<td>Having enough physical activity (n, %)</td>
<td>80 (42.1%)</td>
</tr>
<tr>
<td>Having sufficient money for medicines (n, %)</td>
<td>104 (54.7%)</td>
</tr>
</tbody>
</table>

<sup>1</sup>Percentages do not always match the total number of patient because of the missing answers.
<sup>2</sup>There is no statistical difference between the subgroups.
normal systolic BP higher than 140 mmHg (Subgroup 2). The patients gave information if they had experienced symptoms at lower BP levels than those preferred. Symptoms were categorized as weakness, dizziness, nausea, headache, sweating, heat and visual disturbances. Nevertheless, majority of the patients would not take medicine as prescribed if they were asymptomatic for increased BP at the time.

All the data were analyzed using statistical package for social sciences (SPSS) version 17 (SPSS inc, Chicago, IL, SAD). Normal distribution of continuous variables was considered if skewness was < 1. Mean values of continuous variables were categorized as mean ± standard deviation for normal distribution of variables, but if variables were not normally distributed, or a sample size was too small, then the median and range were used. Nominal variables were shown as frequencies and percentages. Independent-sample T-test was used to compare the means of between two groups of patients for normally distributed data. The Mann-Whitney test was used as test for assessing the difference between two independent . Chi-square test was used to determine differences among two independent samples for normal data. The differences were considered significant when P-value was <0.05. Because of the missing answers, the percentages do not always match the total number of the patients. 17 patients died during the implementation of the study. Other patients could not provide answer due to their poor mental or physical status. They were also included in the analysis, when possible. Thus, we considered some unanswered questions as missing, rather than dropped out cases, while the study was of cross-sectional type.

RESULTS

202 chronic HD patients were included in the study. Regarding the patients’ perception of BP values, we divided the subjects into the two groups: patients who considered maximum normal systolic BP to be up to 140 mmHg (Subgroup 1) and patients who considered maximum normal systolic BP to be higher than 140 mmHg (Subgroup 2). Mean age was 64±13 years, age range from 25 to 85 yrs. Patients that didn’t have appropriate view on normal BP were older (65±12 years) in comparison with those with correct BP perception (60±13 years); (t=–2.546, P=0.012). There was no statistical difference in other patients’ characteristics between the stated subgroups. No difference in the opinion on normal arterial blood pressure value was found between 91 patients coming from rural (45%) and 111 patients from urban (55%) area, either. Underlying renal disease was chronic glomerulonephritis in 56 subjects, chronic interstitial nephritis in 49 subjects, autosomal dominant polycystic kidney disease in 12 subjects, diabetes mellitus in 40 subjects, AH in 27 subjects and other underlying renal disease in 5 subjects, while an unknown underlying renal disease was recorded in 13 subjects. The differences between the two subgroups are shown in Table 1. Median duration of HD for all participants was 4 years, range 0–26; mean duration of AH was 15±11 years; median of the treatment of AH was 10 years, range 0–26. All patients were considered to suffer from AH, for they were prescribed antihypertensives at least for some time during their illness.

TABLE 3

Declared maximum normal systolic blood pressure, current number of antihypertensive drugs, mean systolic blood pressure and delayed arterial hypertension treatment between the two subgroups divided according to the declared maximum systolic BP (cut-off 140 mmHg).

<table>
<thead>
<tr>
<th>Declared maximum normal systolic BP</th>
<th>n (%)</th>
<th>Declared maximum systolic BP (n, mmHg)</th>
<th>Mean systolic BP (n, mmHg)</th>
<th>Current number of antihypertensive drugs</th>
<th>Delayed AH treatment (n, years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;140 mmHg</td>
<td>61 (30.2%)</td>
<td>median 130 range 100–135</td>
<td>136±15</td>
<td>median 2 range 1–5</td>
<td>median 0 range 0–28</td>
</tr>
<tr>
<td>≥140 mmHg</td>
<td>116 (57.4%)</td>
<td>median 150 range 140–180</td>
<td>143±16</td>
<td>median 3 range 1–11</td>
<td>median 0 range 0–40</td>
</tr>
</tbody>
</table>

1\text{Z}=−11.227, P<0.001; Mann-Whitney test
2\text{t}=–2.463, P=0.015;
3\text{Z}=–2.025, P=0.043; Mann-Whitney test
4\text{Z}=–2.088 P=0.037; Mann-Whitney test
tolic BP to be higher than 139 mmHg (median 150 mmHg, 140–180); z = −11.227, \( p < 0.001 \), (Mann-Whitney test). Mean systolic BP for all participants was 140 ± 16 mmHg but, when we divided them based on their view on BP values, Subgroup 1 had lower systolic BP (136 ± 15 mmHg) than Subgroup 2 (143 ± 16 mmHg); t = −2.463, \( P = 0.015 \). There were significantly more patients with systolic BP ≥ 140 mmHg in Subgroup 2 (63.6%) than in Subgroup 1 (43.1%); Chi-square = 6.396, \( P = 0.011 \). Patients that didn’t have appropriate view on normal BP were taking more antihypertensive drugs (median 3, range 1–11) than those in Subgroup 1 (median 2, range 1–5); z = −2.025, \( P = 0.043 \), (Mann-Whitney test).

Table 4 shows the number of used antihypertensive drugs. Majority of patients were taking more than one antihypertensive drugs. Among the antihypertensive drugs used in therapy, there were beta-blockers in 39.1%, alpha-blockers in 17.3%, RAAS inhibitors in 40.1%, vasodilators in 28.2%, diuretics in 21.3% and calcium channel blockers in 47% of the patients. Table 5 shows the distribution of prescribed antihypertensive drugs. 17.3% of all 202 patients started their antihypertensive treatment with delay, even up to 40 years. In Subgroup 2, the year of AH diagnosis differed significantly from the year of the beginning of the treatment than in Subgroup 1; z = −0.288, \( P = 0.037 \), Mann-Whitney test (Table 3). Most of the patients (55%) would not take antihypertensives when BP was lower than that preferred.

Table 6 shows mean BP values during three consecutive HD sessions. In Subgroup 2, the patients had higher predialysis MAP (104 ± 10 mmHg) than in Subgroup 1 (101 ± 9 mmHg); t = −2.362, \( P = 0.019 \), while the difference was not significant between the middle and the end-dialysis MAP. However, patients in Subgroup 2 had intradialytic hypotension less frequently (60.5%) than in Subgroup 1 (76.3%); Chi-square = 4.289, \( P = 0.038 \). 92% of 202 patients reported symptoms during that lower BP than the preferred (Figure 1).

**DISCUSSION**

The primary aim of every medical therapy is to achieve beneficial outcome. Both healthcare professionals and patients must make effort to accomplish this goal. Therapeutic compliance includes not only the patient’s compliance with medication but also with diet, exercise, or lifestyle changes. Increasing attention is being given to functional health literacy, which is defined as ability to understand and act on health information. Even 30% of 202 interviewed patients at University Hospital Centre Osijek were not compliant with antihypertensive treatment. Most of the patients (55%) would not take antihypertensives when BP was lower than that preferred. It still remains uncertain if our patients had poorly regulated AH, due to insufficient compliance with antihypertensive therapy or they were adapted to increased BP. The question remains whether this was a consequence of the frequently delayed AH treatment or of non applicable guidelines for this particular population of patients. A randomized controlled trial by Hayden B. Bosworth et al. compared two groups of patients in which the first group underwent 24-month tailored behavioral and educational intervention by telephone to achieve adequate BP control, and the second group was a...
control group with no interventions. In the six-month preliminary outcomes, intervention group had a 9% increase in a self-reported medication adherence, while the increase in the control group was only 1% (30). Our main objective was to determine whether a distorted view on normal BP values had influence on patients’ compliance. 57.4% of chronic HD patients at University Hospital Centre Osijek hold considered increased BP values for normal, which could result in their poor BP control. Nevertheless, the patients preferring increased BP were older and seemed to be somehow adapted to elevated BP. Vanessa A. Brown and colleagues found that only 30% of patients in the general population were identified as controlled and that the lack of goal complexity and self-care may be due to the older age of participants and influences related to generational cohort (31). Among HD patients, limited observational data indicate that the relationships between BP and age may differ from that of the general population. A study by Rohrscheib et al. shows that systolic and diastolic BP is elevated in young HD patients and declined slightly in the elderly. This could be explained by greater arterial stiffness at any age in HD patients that in the general population. A study by Rohrscheib et al. shows that systolic and diastolic BP is elevated in young HD patients and declined slightly in the elderly. This could be explained by greater arterial stiffness at any age in HD patients that in the general population. A study by Rohrscheib et al. shows that systolic and diastolic BP is elevated in young HD patients and declined slightly in the elderly. This could be explained by greater arterial stiffness at any age in HD patients that in the general population. A study by Rohrscheib et al. shows that systolic and diastolic BP is elevated in young HD patients and declined slightly in the elderly. This could be explained by greater arterial stiffness at any age in HD patients that in the general population. A study by Rohrscheib et al. shows that systolic and diastolic BP is elevated in young HD patients and declined slightly in the elderly. This could be explained by greater arterial stiffness at any age in HD patients that in the general population. A study by Rohrscheib et al. shows that systolic and diastolic BP is elevated in young HD patients and declined slightly in the elderly. This could be explained by greater arterial stiffness at any age in HD patients that in the general population. A study by Rohrscheib et al. shows that systolic and diastolic BP is elevated in young HD patients and declined slightly in the elderly. This could be explained by greater arterial stiffness at any age in HD patients that in the general population.

### TABLE 6
Blood pressure values during hemodialysis session

<table>
<thead>
<tr>
<th>Value</th>
<th>All patients (N=202)</th>
<th>Declared maximum normal BP &lt;140 mmHg (n=61)</th>
<th>Declared maximum normal BP ≥140 mmHg (n=116)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predialysis MAP (n, mmHg)</td>
<td>104±10</td>
<td>101±9</td>
<td>104±10</td>
</tr>
<tr>
<td>Mid dialysis MAP (n, mmHg)</td>
<td>99±10</td>
<td>98±11</td>
<td>99±9</td>
</tr>
<tr>
<td>End dialysis MAP (n, mmHg)</td>
<td>101±10</td>
<td>100±10</td>
<td>102±10</td>
</tr>
<tr>
<td>Intradialytic hypotension (n, %)</td>
<td>126 (67%)</td>
<td>45 (76.3%)</td>
<td>69 (60.5%)</td>
</tr>
</tbody>
</table>

1Mean of the three mean arterial pressure (MAP) levels measured by three consecutive HD sessions.
2P = 0.019, t=−2.362; 3Chi-square = 4.289, P = 0.038
-hemodialysis values is marginally better than both (40). BP obtained during dialysis should be used to ensure hemodynamic stability and home BP monitoring for diagnosing and treating hypertension among HD patients (41). The mean arterial pressure (MAP) is often used as an expression of BP in HD patients, instead of using solely systolic or diastolic BP. In our study, all subjects had normal predialytic MAP below 107 mmHg (recommended by the guidelines), but predialysis MAP was higher (104±10 vs. 101±9, P=0.019) in patients with inappropriate view on BP values. Those patients had surprisingly less frequently intradialytic hypotension (60.5% vs 76.3% in Subgroup 1), since the lower MAP is more frequently associated with intradialytic hypotension, which might in turn be prevented or treated with hypernatriemic dialyse, frequent cessation of ultrafiltration, and saline infusions. Patients considering elevated BP value for normal and consequently not taking antihypertensives as prescribed could have influenced the occurrence of intradialytic hypotension. Intradialytic hypotension not only causes discomfort, but also increases mortality. According to recent data, a low post-dialytic BP was associated with significantly increased risk for mortality (42). Thus, non-compliance under such circumstances could be considered as rational, aimed to prevent even worse complication, i.e. hypotension. Survival analysis comparing long-term outcome in patients prone to intradialytic hypotension should be conducted between those so-called non-compliant, for not taking antihypertensives regularly to avoid hypotension during dialysis, and those strictly adherent to the medication, irrespective of the blood pressure instability during HD session. That would weigh the risk of the two harmful situations.

CONCLUSION

Chronic hemodialysed patients consider normal BP values to be higher than those officially recommended. Most of them had poorly regulated AH and did not take antihypertensives regularly. It might be, at least in part, due to insufficient compliance with antihypertensive therapy. Except for the ignorance, the different view on normal BP and non-compliance could be contributed to the symptoms they were experiencing when BP was below the reported preferred values. Except from those with distorted view on hypertension, non-compliance could probably be expected from not a small proportion of severely ill patients who were not able to make opinion on the subject. Nevertheless, the patients preferring higher BP were older and seemed to be somehow adapted to elevated BP. The question remains whether this is a consequence of frequently delayed AH treatment or non applicable guidelines for this particular population of patients.

REFERENCES

27. KLEINSINGER F 2010 Working with the noncompliant patient. The Permanente Journal 14 (1).