Hypertension in the haemodialysis population: any relationship to 2-years survival?

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Abstract

Hypertension is present in 72% of 649 patients surveyed. We followed these patients longitudinally for 2 years. We have reported earlier on the lack of adverse effects of hypertension on 1-year mortality in a cohort of 649 patients [5]. We report here on their survival at 2 years and its relation to their blood pressures after adjusting for age, diabetes mellitus, serum albumin, and race.

Methods

We reviewed the complete computerized files on 649 HD patients enrolled in 10 haemodialysis centres in the state of Mississippi, USA. One-month dialysis records for each patient from mid-October 1994 to mid-November 1994 were reviewed. Predialysis mean arterial pressure was calculated as immediate predialysis diastolic pressure plus one-third the difference between systolic and diastolic pressure. Patients were classified as hypertensive if their average pre-MAP was more than 114 mmHg or they were receiving antihypertensive drugs during the study period. Normotensives had a pre-MAP <114 and were not receiving any antihypertensives. We followed these patients for 2 years to determine their survival and the effect of their BP status, as determined in October 1994, on 2-year mortality.

Results

In univariate analysis, hypertension was associated with improved 2-years survival (relative risk 0.64, \( P = 0.08 \) compared to normotensives). Furthermore, among the hypertensives, good blood pressure control (less than 140/90) was associated with increased relative risk of death at 2 years (RR 1.86, \( P = 0.004 \)). In multivariate analysis, taking age, race, serum albumin, and diabetic status into consideration, there was a 27% reduction in mortality among hypertensives compared to normotensives (RR 0.73, \( P = 0.06 \)). Other factors of significance in multivariate analysis were age (RR 1.03/year, \( P = 0.02 \)), serum albumin (RR 0.36/g, \( P < 0.0001 \)), diabetes mellitus (RR 1.35, \( P = 0.07 \)), and race (RR 0.64, \( P = 0.05 \)).

Conclusions

Our study suggests that hypertension has no adverse effect on survival at 2 years in the haemodialysis population.

Key words: antihypertensives; chronic renal failure; end-stage renal disease; haemodialysis; hypertension; mortality; survival

Introduction

Recent studies have highlighted the magnitude of hypertension in the HD population. The impact of hypertension on mortality in HD patients has, however, not been well studied. Retrospective analyses have suggested that the key to long-term survival is elimination of hypertension [1,2]. Charra et al. [3] have found reduced survival when predialysis mean arterial pressure (pre-MAP) was above 99 mmHg. In a previous publication [4], we have shown that hypertension is present in 72% of 649 patients surveyed. We followed these patients longitudinally for 2 years. We have reported earlier on the lack of adverse effects of hypertension on 1-year mortality in a cohort of 649 patients [5]. We report here on their survival at 2 years and its relation to their blood pressures after adjusting for age, diabetes mellitus, serum albumin, and race.

Subjects and methods

Patients

We reviewed the complete computerized files on 649 HD patients enrolled in 10 haemodialysis centres in the state of Mississippi, USA. All 10 units are run by Kidney Care, Inc. Jackson, MS. One-month dialysis records for each patient from mid-October 1994 to mid-November 1994 were reviewed. This is equivalent to 14 dialyses and 14 predialysis BP readings for each patient. Pre-MAP was calculated as immediate predialysis diastolic pressure plus one-third of the difference between systolic and diastolic pressures. Patients were classified as hypertensive (Hyper) if their average pre-MAP was more than 114 mmHg or they were receiving antihypertensive drugs during the study period. Normo-
tensives (Normo) had a pre-MAP <114 and were not receiving any antihypertensives. Causes of end-stage renal disease were identified from patient’s records as reported by those on one antihypertensive drug. Calcium-channel-blockers were the most commonly used (in 48% of those on one antihypertensive drug) followed by direct vasodilators (20%) and sympatholytics (20%). The least used was angiotensin-converting enzyme inhibitors (in 12% of those on one antihypertensive drug).

Statistics

The unpaired Student t-test was used for comparisons involving only two groups. We used the Cox proportional hazard model to assess relative risk in both univariate and multivariate analyses. Unless otherwise stated, all data are reported as the mean ± SD and P value <0.05 was considered significant. Statview computer software (Abacus Concepts, Inc. Berkeley, CA 1992) was used.

Results

Description of the study population: (Table 1)

Demographics, dialysis duration, ranges of blood pressure, and and reported causes of ESRD in the total study population as well as in the hypertensives and normotensives are shown in Table 1. All patients were dialysed with cuprophone-based dialysers. The average dialysis session was 236 min (approximately 4 h) three times a week. The average urea reduction ratio was 0.59. The predialysis MAP was 111 ± 11 mmHg for the total population. Four hundred and sixty-seven patients (71.9% of total study population) were hypertensive with an average pre-MAP of 115 ± 11 mmHg; 381 (81.5%) of the hypertensives were receiving antihypertensive drugs while 86 patients (18.5%) were not; 220 patients (47.1% of the hypertensives) were receiving one antihypertensive drug; 132 (28.2%) were receiving two antihypertensive drugs, while 29 patients (or 6.3%) were receiving three or more drugs. Among the group receiving one antihypertensive drug, calcium-channel-blockers were the most commonly used (in 48% of those on one antihypertensive drug) followed by direct vasodilators (20%) and sympatholytics (20%). The least used was angiotensin-converting enzyme inhibitors (in 12% of those on one antihypertensive drug).

Univariate analysis: (Table 2)

After 24 months of follow-up we observed 157 deaths; 435 patients were alive; 34 patients were lost to follow-up, and 23 had been transplanted. Live patients were censored at 24 months, at the time of transplant or loss to follow-up. At the end of 2 years follow-up, there were 57 deaths among the 191 normotensives (29.8%) and 100 deaths among 458 hypertensives (21.8%). Table 2 shows the results of univariate analysis. Gender did not appear to affect survival. Blacks fared better than whites (relative risk of death at 2 years was 0.51, \( P = 0.003 \)). Age was the most important factor adversely affecting survival. For each year increase in age, risk of death was increased by 3%. Albumin also strongly influenced survival. Each 1-g increase in albumin decreased RR 70%, \( P < 0.0001 \). Diabetes mellitus was associated with an increased relative risk of 1.52, \( P = 0.01 \). Urea reduction ratio (URR) had no influence on survival (URR < 0.65 group had a relative risk of dying of 0.94, \( P = 0.83 \)). There was no difference in survival according to the time on dialysis at baseline (Table 2). Hypertensives with an average pre-MAP of 115 mmHg fared better than normotensives (average pre-MAP 101 mmHg); relative risk of dying at 2 years for the hypertensives was 0.64, \( P = 0.008 \). Furthermore, among the hypertensives, good blood pressure control (less than 140/90 or pre-MAP < 106 mmHg) was associated with increased relative risk of death at 2 years (RR 1.86, \( P = 0.004 \)). Patients were then divided into five groups according to their actual level of BP at baseline (Table 3). This classification corresponds to the stages

Table 1. Characteristics of the study population

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Hypertensives</th>
<th>Normotensives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>649</td>
<td>458</td>
<td>191</td>
</tr>
<tr>
<td>Males (n (%))</td>
<td>305 (47)</td>
<td>219 (47)</td>
<td>86 (45)</td>
</tr>
<tr>
<td>Females (n (%))</td>
<td>344 (53)</td>
<td>239 (53)</td>
<td>105 (55)</td>
</tr>
<tr>
<td>Blacks (n (%))</td>
<td>583 (89)</td>
<td>409 (89)</td>
<td>174 (91)</td>
</tr>
<tr>
<td>Whites (n (%))</td>
<td>66 (11)</td>
<td>49 (11)</td>
<td>17 (9)</td>
</tr>
<tr>
<td>Age in years</td>
<td>56 ± 15</td>
<td>60 ± 15</td>
<td>60 ± 15</td>
</tr>
<tr>
<td>Time on dialysis in months</td>
<td>49 ± 50</td>
<td>46 ± 47</td>
<td>55 ± 57</td>
</tr>
<tr>
<td>Diabetics (n (%))</td>
<td>191 (29)</td>
<td>132 (29)</td>
<td>59 (30)</td>
</tr>
<tr>
<td>Predialysis range of systolic BP</td>
<td>78–223</td>
<td>114–223</td>
<td>78–170</td>
</tr>
<tr>
<td>Predialysis range of diastolic BP</td>
<td>51–130</td>
<td>55–130</td>
<td>51–95</td>
</tr>
<tr>
<td>Predialysis MAP</td>
<td>111 ± 12</td>
<td>115 ± 11</td>
<td>101 ± 8</td>
</tr>
<tr>
<td>Cause of ESRD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension (n (%))</td>
<td>331 (51)</td>
<td>248 (54)</td>
<td>84 (44)</td>
</tr>
<tr>
<td>Diabetes mellitus (n (%))</td>
<td>191 (29)</td>
<td>132 (29)</td>
<td>59 (30)</td>
</tr>
<tr>
<td>Glomerulonephritis (n (%))</td>
<td>51 (8)</td>
<td>34 (7)</td>
<td>16 (9)</td>
</tr>
<tr>
<td>Polycystic kidney disease (n (%))</td>
<td>12 (2)</td>
<td>3 (1)</td>
<td>9 (5)</td>
</tr>
<tr>
<td>Others (n (%))</td>
<td>64 (10)</td>
<td>41 (9)</td>
<td>23 (12)</td>
</tr>
</tbody>
</table>
defined by the Joint National Committee on the Prevention and Treatment of Hypertension in its fifth report [6]. There was a gradual consistent increase in relative risk of dying as the BP increases. The severe hypertensives had the best survival and were used as the reference group. Moderate hypertensives had a RR of 1.52, mild hypertensives RR 1.71, high normal BP 2.46 and normal BP group 2.59. The reduced RR of hypertension was only true for blacks (Table 4) which constituted the vast majority of our population (89%). In whites there was an increased risk of dying among the hypertensives that did not reach statistical significance (RR 1.4, $P=0.44$).

**Multivariate analysis: (Table 5)**

In multivariate analysis (similar to univariate analysis), only increasing age and low serum albumin were associated with increased RR of dying. There was a trend towards increased mortality in the diabetics (RR 1.3, $P=0.07$). Black race had a favourable effect on survival that was marginally statistically significant (RR 0.64, $P=0.05$). BP was not an independent factor affecting 2-year survival. Indeed there was a reduced relative risk of dying in the hypertensives compared to the normotensives that did not reach statistical significance (RR 0.73, $P=0.06$).

**Discussion**

Our study agrees with several prior studies [7] showing increasing age, diabetes mellitus, and low serum albumin to have an adverse effect on survival in the HD population. We have shown in this study that hypertensive HD patients have a better 2-year survival than the normotensives. The improved 2-year survival was evident but less significant after adjusting for all other variables that were significant in univariate analysis. Most importantly, we did not find any adverse effect of high blood pressure on 2-year survival in our cohort of haemodialysis population. The improved survival was gradual and consistent as the blood pressure increased at all levels and stages of blood pressure. There did not appear to be a certain cut-off BP point below which survival decreased. Thus, we do not believe that the reduced survival of the normotensives is related to an underlying heart failure causing relative
lowering of the blood pressure and acting as a confounding variable increasing mortality. Furthermore, we used the blood pressure at baseline to avoid the pre-terminal lowering of blood pressure in sick patients who are slowly deteriorating from underlying cardiovascular disease. Similar conclusions were reached in a recent study by Iskei et al. [8] who found that the lower the diastolic blood pressure, the higher the mortality, in a group of 1243 haemodialysis patients. Earlier studies looking at effect of hypertension on survival in the HD population are few. In a recent study from Japan [9] comparing 132 HD patients who survived to 46 patients who died during a 3-year follow up, survivors had a lower systolic BP than non-survivors. Diastolic BP did not differ. Neff et al. [10] compared 37 patients who survived 10 years on haemodialysis to 103 patients who died, and found a tendency towards lower BP in the survivors that was not statistically significant. In a study of 104 patients from Uruguay [11] who were followed for 3 years, a pre-MAP >115 mmHg was associated with twice the risk of treatment failure (defined as death or admission to hospital). However, only seven patients died and there is no separate analysis for mortality as distinguished from admission to hospital.

We believe our study differs from all the above studies because we took into consideration the multiple factors that affect survival and did not study the effect of BP in isolation. Furthermore, we studied a large number of patients in a longitudinal prospective fashion after establishing their BP status at baseline. Charra et al. [3], in a recent analysis of the survival data on 769 patients dialysed in one centre in south France, found that for each 1 mmHg increase in predialysis MAP the risk of death increases by 3.9% (39% for 10 mmHg). We found a reduction in relative risk of 4% for each 1 mmHg increase in pre-MAP. It is of note that only 2% of the south France patients were receiving antihypertensives as compared to 59% of our patients. Antihypertensives may well have improved the prognosis of our hypertensive patients. This may be related to amelioration of the excessive swings in the blood pressure and sympathetic system activation during dialysis. The difference may also relate to length of follow up (much longer in Charra’s series) and the population studied. Most of Charra’s patients were whites as compared to 89% blacks in the current study. Indeed this is supported by our observation that among the 66 white patients in our study, there was an increase in RR (albeit statistically insignificant) among white hypertensives while hypertension in blacks was associated with reduced mortality.

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References


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