Is Hypertension Beneficial to the Conventional Hemodialysis Patient?

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Hypertension is common in the conventional hemodialysis population. While hypertension in the general population has been shown to reduce survival, the issue is less clear in the dialysis population. This review focuses on recent studies showing a favorable outcome in hypertensive hemodialysis patients compared to those with lower blood pressure. Possible explanations for this paradoxical relationship are examined and practical suggestions given for the management of hypertension in the hemodialysis patient.

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Key words

Hypertension, survival, cardiovascular disease

Introduction

Hypertension is common in the hemodialysis population. Recent studies have documented an increasing prevalence of the disease. While earlier studies [1] have shown a prevalence of no more than 15% after starting dialysis, more recent studies document a prevalence of 72% or more. A 1992 report of the European Dialysis and Transplant Association [2] found a prevalence of 83%. Salem [3] documented a prevalence of 72% in 649 patients from the southeast United States. The United States Renal Data System (USRDS) 1999 report estimates that 75% of patients on dialysis in the U.S. are hypertensive [4]. This is alarming in view of the known effects of hypertension on morbidity and mortality in the general population. An analysis of nine prospective studies in the general population showed a linear correlation between level of blood pressure (BP) and relative risk of stroke and coronary heart disease [5]. In addition, the hemodialysis population suffers an excess of cardiovascular mortality. In the USRDS analysis of 1993, the relative risk of cardiovascular mortality was several fold higher in the dialysis population compared to the general population for all age groups [6]. Relatively young dialysis patients in the 25- to 34-year age range had 10 times the likelihood of death from cardiovascular disease compared to the general population of similar age. The average dialysis patient has a multitude of underlying cardiac diseases at the start of and during his dialysis life. Parfrey and Foley [7] have shown that only 16% of these patients have a normal echocardiogram, 48% suffer from congestive heart failure, and 32% have an underlying ischemic heart disease. These abnormal echocardiographic findings detected by Parfrey and Foley [7] were strongly correlated with mortality. The 6-year survival in the group with normal echocardiograms was around 70%, while only 10% of those with systolic dysfunction survived for 6 years. Charra *et al*. [8] from France have found that the key to long-term survival is control of BP. At 5, 10, 15, and 20 years, normotensive patients survived longer than hypertensive patients. In another study, Tomita *et al*. [9] found that patients who survived for 3 years on dialysis had a lower systolic BP than nonsurvivors. There was no difference in diastolic pressure between the two groups.

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The emerging paradox of survival

In contrast to the above statements, and as early as 1993, the USRDS data analysis showed a favorable survival trend for the hypertensive dialysis patient compared to the normotensive patient [6]. In this study, higher systolic pressure was associated with better survival, even after adjustment for case mix and laboratory variables. In a subsequent report, Salem and Bower [10] analyzed the survival pattern of a cohort of 649 patients at 1 year. It appeared from their analysis that the hypertensives fared better than the normotensives in a nonselected group of U.S. hemodialysis patients. Indeed, compared to normotensives, hypertensives had half the risk of dying. This survival advantage seemed to be related to the use of antihypertensives. The hypertensives on treatment had half the risk of dying compared to the normotensives. The untreated hypertensives' survival was similar to the normotensives'. In addition, treated hypertensives survived better than nontreated hypertensives, despite similar BP levels. It appeared that the BP level *per se* had limited effect on survival. Analysis of 2-year survival [11] in the same cohort of patients revealed a tendency toward better survival for hypertensives (relative risk of dying was 0.73, $p = 0.06$). The authors noted a gradual decline in mortality as BP rose from normotensive to high normal, mild hypertension, moderate hypertension, and severe hypertension. The adverse effect of lower BP was noted at all levels and not only in the hypotensive group. These results were surprising and difficult to explain.

In 1996, Duranti *et al*. [12] published their survival data as it related to hypertension in a group of 370 dialysis patients followed for 24 years. No difference was found between normotensives and hypertensives. That paradox was further confirmed by Iseki *et al*. [13] in 1200 Japanese dialysis

patients. As the diastolic BP rose from 70 to more than 100 mm Hg, so did chances of surviving 5 years. Iseki *et al*. [13] calculated that, for every 10 mm Hg rise in diastolic BP, mortality was reduced by 17%. Zager *et al*. [14] came to similar conclusions, but also found a "U"-shaped relation between postdialysis systolic BP and survival. Those with a postdialysis systolic pressure below 120 or above 180 mm Hg fared worse than patients with a postdialysis BP between 120 and 180 mm Hg. Port *et al*. [15] came to similar conclusions in their analysis of the USRDS data published in the *American Journal of Kidney Diseases* in 1999.

The use of the postdialysis BP in the above two studies is subject to questioning in view of its dependence on fluid removal and its tendency to change rapidly in the few hours after dialysis.

Discussion

So, what do we make of this paradoxical relationship? There are several possible explanations for this situation. It may be that the normotensives are the ones with underlying cardiac disease and/or congestive heart failure explaining their high mortality. In other words, the heart disease is associated with relative normotension and predisposes to the increased mortality observed, thus acting as a confounding factor. Foley *et al*. [16] reported in 1996 that those with the lowest BP were the older patients with higher prevalence of heart disease and diabetes. The authors concluded that the association of low BP with mortality was a marker for having had cardiac failure prior to death. However, Port *et al*. [15] reported an advantage for the hypertensive dialysis patient even after adjusting for these factors. It is noteworthy that the report by Port *et al*. [15] depended on data reported to the USRDS and is likely less reliable than the direct clinical observations of Foley *et al*. [16].

Another possible explanation is that the blood vessels in dialysis patients are already atherosclerotic and the higher BP is required for adequate tissue perfusion. Duranti *et al*. [12] have shown that young normotensives (with less atherosclerosis) survive better than hypertensives. On the other hand, in the over-age-50-years group, hypertensives did better than normotensives. In other words, treatment of the young hypertensive dialysis patient may confer protection, while the older hypertensive may be harmed by lowering the BP. The threshold for defining hypertension in the above mentioned study was a BP higher than 150/90 mm Hg.

The presence of coronary artery disease may indeed require a higher diastolic perfusion pressure for appropriate systolic function. In addition, rapid lowering of BP in patients with left ventricular hypertrophy may lead to coronary ischemia [17]. This is similar to what happens during dialysis sessions when BP is rapidly lowered by ultrafiltration.

Another issue that needs resolution is to what extent should BP be lowered in these patients. A recent reanalysis of the Framingham data [18] suggests that, below a threshold BP (dependent on sex and age), there is no benefit to antihypertensive treatment. This threshold might be much higher than previously thought. For example, a systolic pressure of 160 mm Hg in a man of 65 years is acceptable. It may be that the conventional wisdom of adding age to 100 for determining systolic BP is still appropriate. This is particularly important in patients with severe underlying coronary and cerebral atherosclerosis.

Dialysis patients have many risk factors for cardiovascular disease. Hypertension is only one of these factors. Indeed, for a similar level of BP, the risk of cardiovascular mortality in the general population varies by as much as 14-fold [19]. Hypertension may not be the only cause for the high cardiovascular mortality prevalent in these patients, and we need to address the situation as a whole. For example, underlying ventricular dysfunction, hyperparathyroidism, dyslipidemia, uremic factors, aortic distensibility, *etc*. may also have an important role in the causation of cardiovascular disease in these patients. In an elegant study of the effect of atherosclerosis on survival of the hemodialysis patient, Blacher *et al*. [20] divided 241 patients into three groups depending on their aortic stiffness (as determined by pulse wave velocity measurements). The patients with the stiffest aortas had the worst survival, irrespective of their BP level.

To complicate matters even more, we are still not sure which BP measurement to treat. Most nephrologists depend on predialysis systolic BP. However, a recent study [21] found the 20 minutes postdialysis BP to correlate best with the interdialytic, average ambulatory BP. Based on these findings, we may be overtreating a significant proportion of these patients.

It is clear that more studies are needed to clarify the above issue and to provide sound clinical advice with respect to management of these sick patients. These studies need to be prospective and aim to lower the BP to different levels using different classes of drugs to answer some of the above questions.

Conclusions

The effects of hypertension on survival of the hemodialysis population are unclear at present. There is a possibility that aggressive control of BP in this population to levels desirable in the general population may be detrimental, at least in a subset of patients. Allowance for higher BP is advisable in the older atherosclerotic patient with underlying cardiac disease. Further prospective studies are essential before specific recommendations can be given with respect to level of BP control.

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