Can antihypertensive medications control BP in haemodialysis patients: yes or no?

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In the April 1999 issue of Nephrology Dialysis Transplantation, there is an article which summarizes the report of the US task force convened to study the epidemic of cardiovascular disease in the haemodialysis population [1]. This task force, composed of prestigious experts, collectively made a report on what to do about the growing epidemic of cardiovascular disease in the haemodialysis population. On page 832, in the all important ‘treatment of hypertension’ section, this summary article contains the following statement: ‘All classes of anti-hypertensive agents are effective with the exception of diuretics’. If that statement is true, how come greater than 65% of the world’s haemodialysis patients are hypertensive [2–6]? 

In this same April 1999 issue, beginning on page 919 is a report of a study by Innes et al. [7]. This study compares the mortality between two top quality haemodialysis centres. One is located in Nottingham, UK, the other in Tassin, France. This comparison clearly demonstrates that patient survival is much better in the French dialysis unit than in the dialysis unit in England. After careful analysis of all relevant risk factors such as age and comorbidity, the authors conclude that the main identifiable factor, which could explain this difference in survival, is a marked difference in blood pressure among the patients from each unit. In Nottingham, most patients had chronic hypertension; in Tassin, which uses the drug free dry weight method of BP control [8], BP of almost all their patients was in the low normal range.

This important comparison of survival results between Nottingham and Tassin also is of great interest because of the type of patients that did not show a difference in survival. These groups included diabetics and patients who began dialysis with severe cardiovascular co-morbidity. One would not expect control of BP to significantly prolong life in these groups because they already have advanced atherosclerosis and do not survive long enough to give BP control a chance to stabilize or perhaps reverse this condition. In the Framingham study [9], it took a minimum of 10 years for the benefits of normalizing BP to show an effect on patient survival. Thus, conclusions from papers like that of Zager et al. [10] are misleading. These authors, based on a 2.5-year study, concluded that: ‘Establishing optimal BP targets in patients will require a multicentre randomized controlled clinical trial that includes serial electrocardiograms, 48 h APBM’s and information on antihypertensive medications’. Such a conclusion is unwarranted when one considers the mountain of evidence that supports the proposition that long-term control of hypertension uniformly helps to prevent the development of atherosclerosis.

However, in some dialysis patients with a life expectancy of less than 5 years due to age and/or comorbidity, aggressive treatment to try and control BP may represent a distraction and perhaps even be harmful. This idea is supported by a recent study of Port et al. [11] and editorial comments by Salem [12]. In Port’s study, a low (<110 mmHg) pre-dialysis systolic BP was a significant risk factor. According to the authors, this
could be explained by the fact, also emphasized by Foley [13], that hypotension may be a marker of underlying severe heart disease. Other or complementary possibilities are that the low BP and early mortality may be linked to malnutrition, or inadequate dialysis. In chronically ill patients such as these, concentrating on providing a high dose of dialysis with the minimum set at a URR of 0.7 would be most beneficial. At the same time using good clinical judgement can easily solve this problem of the management of BP in haemodialysis patients with a short life expectancy such as diabetics who have rapidly progressive or far advanced cardiovascular diseases. The expensive study called for by Zager [10] is not needed.

If antihypertensive medications are indeed effective in treating hypertension in haemodialysis patients, then why did they not work in Nottingham or in two out of three patients over the world? The fact of the matter is that antihypertensive medications are not only poorly effective in haemodialysis patients but must be discontinued before the dry weight method can be used to control blood pressure [8].

In order to explain my position, I have constructed Table 1. Column one in this table is a hypothesis that divides normal extracellular volume (ECV) into three sub-groups. This hypothesis will need confirmation if, and when, ECV measurements, which are more precise than those currently available, are devised to study this problem of the proposed relationship between small sustained changes in average ECV and BP. The rest of Table 1 is based on published clinical data. In addition, Table 1 helps to clarify the confusion surrounding the meaning of the term ‘dry weight’.

At dry weight, the ECV is normal [14]. Having said that, the problem seems to be that the range of so-called normal ECV is so large that one must hypothesize that there are three levels of normal ECV as far as its effect on BP is concerned. These three levels are shown in column one of the table.

Let us begin the analysis of the information in Table 1 by noting that back in the 1940s before any antihypertensive medications were available, Kempner was able to successfully treat essential hypertension solely by means of reducing the ECV with his rice diet plus the sodium leak of normal kidneys of a few mEq/day [15]. The ECV of Kempner’s normotensive patients was, by isotope measurement, in the normal range [16]. I hypothesize that the ECV of these patients must have been at the low end of normal in order for his rice diet to control essential hypertension. In other words, Kempner’s patients were at what I define as dry weight. This idea assumes that the only way the rice/fruit diet could cure hypertension was by decreasing the size of the ECV. What beneficial role the high potassium intake in the rice/fruit diet had is not clear.

Kempner’s patients ate a diet remarkably similar in sodium content to that of some primitive tribes as described by Fries [17]. Thus, they fit in the same category in Table 1. These tribes have no hypertension and their BP reaches a peak in the mid-twenty age range and declines thereafter as they grow older. Populations in this category remain at dry weight throughout their lives.

Finally, as shown in Table 1, normotensive haemodialysis patients at dry weight have a time averaged ECV which is similar in size as that of primitive tribes who ingest a very low sodium diet or patients with essential hypertension that have been successfully treated by the rice/fruit diet. In the case of dialysis patients, this low normal level of ECV is maintained by the powerful tool, ultrafiltration, which if properly used along with moderate dietary sodium restriction is the only proven method of controlling BP in the haemodialysis population. In my view, the answer to the question posed in the title is ‘no’.

### Table 1. Blood pressure of haemodialysis patients

<table>
<thead>
<tr>
<th>ECV</th>
<th>BP</th>
<th>Response to drug RX</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>High normal</td>
<td>Hypertension</td>
<td>Resistant</td>
<td>Typical dialysis patient</td>
</tr>
<tr>
<td>Normal</td>
<td>Hypertension</td>
<td>Poor</td>
<td>Dialysis patient who develops hypotension due</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>to dialysis because drugs have not been stopped</td>
</tr>
<tr>
<td>Low normal</td>
<td>Normotension</td>
<td>Cannot tolerate</td>
<td>(i) Dialysis patient who is normotensive off</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>drugs [8]</td>
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<td></td>
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<td>(ii) Kempner’s normotensive patients [15]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(iii) Primitive tribes [17]</td>
</tr>
</tbody>
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### References
8. Charras B, Bergström J, Scribner BH. Blood pressure control in
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**Editor’s note**

Please see also the *Original Article* by McGregor et al. (pp. 2676–2679 in this issue).