

The management of hypertension in hemodialysis and CAPD patients

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Abstract

Patients with chronic kidney disease progress to end stage renal disease and about 86% are diagnosed hypertensives. Hypertension is a risk factor for cardiovascular disease which is the main cause of morbidity and mortality in the dialysis population. Pre and post-dialysis blood pressure values of < 140/90 mmHg are recommended as the optimal blood pressure. The extra-cellular volume (ECV) expansion is the main pathophysiological determinant of hypertension in dialysis patients. The efforts should be made to correctly estimate and achieve the patients dry body weight and to limit dietary sodium intake. Angiotensin II receptor antagonists, beta blockers and calcium channel blockers are recommended as first choice drugs. Beta blockers and calcium channel blockers have been associated with reduced cardiovascular mortality and give their protective effects in patients at high risk. Antihypertensive drug therapies can effectively reduce blood pressure and are needed by the vast majority of hemodialysis patients. *Hippokratia 2007; 11 (4): 171-174*

Key words: hypertension, hemodialysis, peritoneal dialysis, cardiovascular disease

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The majority of end stage renal failure patients are hypertensive. Hypertension in the hemodialysis patients population is multifactorial. Optimal blood pressure in dialysis patients is not different from that recommended for the general population, even though definite evidence is not yet available. Pre-dialysis systolic and diastolic BP is of particular importance. Hypertension is associated with an increased risk for left ventricular hypertrophy, coronary artery disease, congestive heart failure cerebrovascular complications and mortality¹. Several therapeutic options are available to normalize BP in these patients such as: short daily hemodialysis, nocturnal hemodialysis, dietary salt and fluid restriction in combination with reduction of dialysate sodium concentration. Studies in hemodialysis patients show that those with the highest blood pressure have the best survival^{2,3}. Available evidence suggests that hypertension should be treated in hemodialysis patients⁴. The purpose of this article is to develop a clinical approach to the management of hypertension in these patients.

Hypertension in peritoneal dialysis

Fifty percent of Peritoneal Dialysis (PD) patients are hypertensives, a rate lower than this in general population and in hemodialysis⁵.

Cardiovascular disease is the most common cause of death, accounting for more than 52% of patients in Renal Replacement Therapy (RRT, USRDS 1998).

The incidence of hypertension in peritoneal dialysis is referred to the 1987 Health National Institute (NIH) CAPD registry in a 12 month observation in PD. Normal BP had 30% of the patients and lower doses of antihypertensives received the 27%. Hamburger RJ, in his published work in *Advances in PD 1989* demonstrates the changes in systolic and diastolic BP one year after commencement

of RRT⁶. BP in CAPD differs statistically significantly ($p < 0.05$) from haemodialysis (HD) and the advantage in controlling BP co exists in peritoneal dialysis patients. In the USA End Stage Renal Disease (ESRD) indicators Project hypertension defined as either systolic BP > 150 mmHg or diastolic BP > 90 mmHg. Fifty three percent of patients in hemodialysis were hypertensives, 34% in CAPD vs 11% in cyclor patients in the same period.

The classification of BP for adults according to NIH JNC VI guidelines are categorized in Table 1:

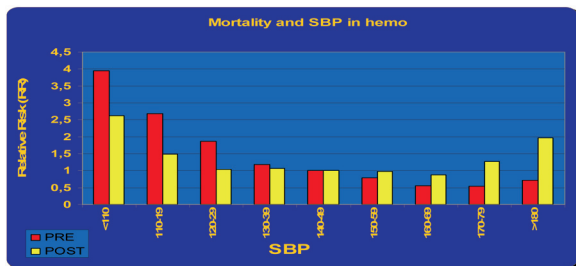
Table 1. Classification of BP for adults according to NIH JNC VI guidelines

	Systolic(mmHg)	Diastolic(mmHg)
Optimal	<120	<80
Normal	<130	<85
High normal	130-139	85-89
Hypertension stage 1	140-159	90-99
Hypertension stage 2	160-179	100-109
Hypertension stage 3	>180	>110
BP target: BP<140/90mmHg		

The influence of PD on BP control is well documented in the Shoda J study⁷. So, the changes in 24-hour BP before and after introduction of PD show a linear decline. The changes in daytime, nighttime and average 24-hour systolic BP, before and after introduction of PD, show a good evidence in BP control with statistically significant difference before and after introduction of PD. A better BP control after the initiation of PD was also noticed in patients with chronic kidney disease.

Patient transfer from HD to PD reveal a statistically significant decline in blood pressure⁷. Lower diastolic BP after one year on dialysis (PD and HD) resulted in better possibility for patient survival⁸. Cardiovascular disease in chronic dialysis patients is increasing over the years⁹. The cause of cardiovascular disease in chronic dialysis pts is multifactorial (Table 2).

Table 2. Mortality risk and systolic blood pressure in hemodialysis patients



Congestive heart failure in pts initiating dialysis in USA show persistently high proportions⁹. The survival in pts with heart failure is worse in comparison with the patients who do not suffer from heart failure on starting RRT⁹⁻¹¹. Cardiovascular disease in peritoneal dialysis patients presents modifiable risk factors such as: bad diabetic control, hypertension, dyslipidemia, hyperhomocysteinemia, calcium and phosphate poor control, treatable sources of inflammation, oxidative stress. Other risk factors exaggerated by PD such are: lipid profile, high insulin levels, poor glycemic control and AGE formation.

Volume control in PD patients is very important to control hypertension. Three year patient survival rates in PD show a better effect according to the sodium and total fluid removal¹². On the other hand the maintenance of residual renal function over time from initiation of PD is of high significance¹³.

Hypertension in hemodialysis

The prevalence of hypertension in hemodialysis patients is about 86%³. Although many patients receive antihypertensive drugs, only 30% have well controlled BP and 12% have untreated hypertension. When ambulatory blood pressure monitoring was used to assess hypertension control in a hemodialysis population the prevalence of systolic hypertension was 73%⁴. The prevalence of systolic hypertension was 37% in an unselected hemodialysis population from the same center⁴. At the time of initiation of RRT the incidence of hypertension was referred to be 90%. After 3-6 months it is referred to be 50-60% in hemodialysis patients, 30% in CAPD patients and 25% in general population^{14,15}.

Hypertension may not be accurately assessed in the general hemodialysis population.

Optimal BP in hemodialysis patients

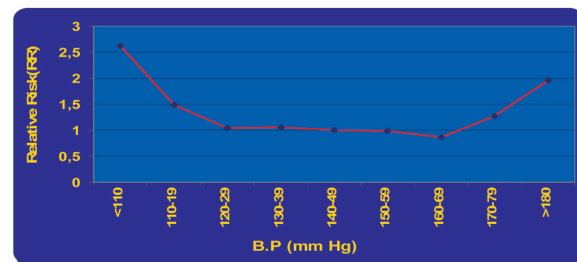
There are three ways in which we can assess the level

of BP in hemodialysis patients. Blood pressure can be obtained before, during and after hemodialysis, by the dialysis staff. This can be done at home by the patient, or by an automatic ambulatory BP monitor.

Optimal blood pressure is defined when pre and post-dialysis BP is < 150/90 mmHg without therapy or the ambulatory day BP monitoring < 135/85 without therapy or the ambulatory nighttime BP monitoring < 120/80 without therapy⁵.

Risk factors that increase the peripheral vascular resistance are: 1) rennin-angiotensin system (RAS), 2) sympathetic nervous system activity, 3) insufficient production of vasodilation substances. Hypertension is the main cause of ischemic heart disease in the general population. Ischemic heart disease is a major cause of death (23%) in hemodialysis patients. Death of ischemic heart disease patients is 17 times higher in dialysis population than in general population in Europe¹⁴. Zager 1998¹⁶, referring to the correlation between cardiovascular disease mortality and hypertension, reported a U curve shape in post-dialysis measurements (Table 2 and Table 3). Zager (1998),

Table 3. Cardiovascular disease mortality and hypertension has U curve shape in hemodialysis patients in Zagers' 1998 reference



published his work of the relative risk of cardiac related deaths in relation to the systolic and diastolic post-dialysis BP. Post dialysis BP is not a proper parameter because it is technically low in extravolume deletion and increases soon after. From these studies we cannot conclude that high blood pressure is related with high mortality in dialysis patients. Actually the opposite exists. Patients with hypertension as primary disease for RRT revealed a relative death risk of 0.86. However the relative death risk for each 1 mmHg increase in pre-dialysis BP, diminishes the cardiovascular relative risk mortality by about 1%¹³. The most impressive finding of this study was the continuous linear decline in mortality with hypertension according to (JNCN) Joint National Category. Port et al, also reported that hypertension is not related to high relative risk mortality in the hemodialysis population². Pre-dialysis SBP < 109mmHg mortality is over 86% (RR 1.86). The higher the BP, the lower the mortality. Diastolic BP does not affect mortality if it is > 110mmHg post-dialysis.

In contrast Charra et al in a retrospective study at the Tassin clinic reported that survival in the hemodialysis population was 20% better when pre-dialysis BP was < 99 mmHg.

Systolic vs diastolic hypertension

Most patients in hemodialysis have systolic hypertension that may or may not coexist with diastolic hypertension¹⁷. Isolated diastolic hypertension is rare⁴. Most dialysis patients are elderly. Even the younger ones have the vascular age of healthy people who are older. A direct relationship between systolic BP and total mortality, and systolic BP and cardiovascular events has emerged in the hemodialysis population¹⁸. Pre-dialysis systolic BP overestimates the mean systolic BP between sessions by about 10mmHg. Post-dialysis BP underestimates the mean systolic BP by about 7 mmHg.

Treatment of hypertension in hemodialysis patients

Free water restriction is a therapeutic option for hyposmolar states, not volume overload. A more appropriate therapy for these patients would be to restrict dietary sodium intake. A two gr sodium diet is commonly recommended. If the patient follows the 2 gr sodium diet, an interdialytic weight gain of 1.25 Kg would be expected over 2 days or 1.9 Kg over the weekend. Only rarely do dialysis patients achieve such small interdialytic weight gains. Limiting weight gain would mitigate the large swings in BP and may ease the intradialytic hypotensive symptoms.

Another source of sodium excess is the dialysate sodium prescription. Individualizing sodium prescription in such patients may be useful. Data points to the usefulness of such a strategy in lowering BP in hypertensive subjects. Lowering dialysate Na based on predialysis plasma Na level, may reduce interdialytic weight gain and thirst. It also may improve BP¹⁹. Treatment recommendations are to: 1) use long duration sessions with low ultrafiltration rate, 2) practice nocturnal hemodialysis, 3) practice short daily sessions.

Drug therapies

The majority of patients with end stage renal disease on chronic dialysis need antihypertensive drug therapy^{17,20}. Several classes of antihypertensive drugs are available and all except diuretics are effective in controlling hypertension in hemodialysis patients. In patients with left ventricular hypertrophy, angiotensin converting enzyme (ACE) inhibitors may be effective in causing regression, although the trial sizes have been limited^{21,22}. Calcium channel blockers (CCBs) are the most widely prescribed class of drugs in patients on hemodialysis^{17,23}. Calcium channel blockers appear to be more effective when the plasma volume is expanded. They do not need additive doses after hemodialysis. Because hypertension in hemodialysis patients is thought to be largely a result of volume expansion, these agents may have a unique advantage in ESRD²⁴. Both dihydro-pyridine^{25,26} and non dihydropyridine calcium channel blockers have unaltered pharmacokinetics in patients with ESRD on hemodialysis and have little dialyzability^{27,28}. Preliminary studies with verapamil have even suggested a reduction in intradialytic hypotension²⁹. Angiotensin converting enzyme in-

hibitors and beta blockers appear to be attractive agents due to their independent cardiovascular benefits. Several other options are available to control hypertension. Transdermal clonidine applied at weekly intervals can improve hypertension control³⁰. Minoxidil, a potent vasodilator, is effective for hypertension control³¹. It should be used with beta blockers to maintain efficacy. The side effects of hirsutism, pericardial effusion, and edema should be carefully monitored³².

To what level BP should be lowered and how is not known. The National Kidney Foundation K/DOQI guidelines suggest that predialysis and postdialysis BPs should be < 140/90 and 130/80 mmHg respectively³³. Studies suggest a mean arterial pressure of < 99 mmHg to be associated with best survival. These patients have long-hours of hemodialysis. Lowering BP too much may render fluid removal during dialysis difficult and may increase the discomfort associated with dialysis. On the other hand, by reducing BP to a lower level some cardiovascular benefits may be realized. An ideal BP in a hemodialysis patient would be associated with: hemodynamic stability during dialysis, orthostatic tolerance after dialysis, the best cardiovascular survival, and optimal health related quality of life. Some of these goals can be achieved by dietary and dialysate sodium restriction. This reduces the amplitude of BP fluctuations but additional factors must be considered. A patient with diastolic dysfunction and left ventricular hypertrophy can experience arterial stiffness and interdialytic hypertension. It is likely that tolerance to BP goals will vary by cardiovascular comorbidities. If there is a true association between hypertension and cardiovascular disease in hemodialysis patients, then the lowest possible home BP with the least symptoms on dialysis and best quality of life may be a prudent goal. This BP goal would need to be individualized. Because a home BP of > 150/90 mmHg correlates with hypertension detected by ABPM, BP targeted to < 150/90 mmHg would be a prudent goal³³.

Unsuccessful therapy

Unsuccessful therapy appears in 62%-72% of patients. The causes are: 1) wrong evaluation of dry weight, 2) overhydration between sessions, 3) unsuccessful drug choices, 4) ineffective low antihypertensive doses (the most common), 5) the practice to discontinue therapy before sessions and 6) wrong pharmaceutical distribution during 24 hours.

Resistant hypertension

When all of the above interventions (pharmaceutical or not) fail, then we must think about: 1) the use of non steroidal anti-inflammatory drugs, 2) renovascular hypertension, 3) increasing cysts in polycystic kidney disease, or 4) no patient compliance. Then we have to deal with using drugs with long term activity like lisinopril or amlodipine, or to increase duration and incidence of sessions, or to transfer patients to CAPD, or to use nephrectomy (unusual).

Paradoxical hypertension

Paradoxical hypertension appears at the end of dialysis when water removal is completed. Pathogenesis and therapy are not well documented. The causes of paradoxical hypertension are: ultrafiltration, hypovolemia, pre-existing hypertension, hypercalcemia, high Ht level, improvement of hypoxia, antihypertensives that are removed during dialysis.

The treatment is: nifedipine per os 10 mg, with quick response or captopril per os 10 mg pre-dialysis, isotonic normal saline NaCl or correction of hypovolemia.

Conclusions

It is important to recognise accurately the hypertensive patients in hemodialysis.

The relationship of hypertension with adverse outcomes is uncertain in the hemodialysis population. If hypertension is an etiologically significant cardiovascular risk factor in hemodialysis patients, the first step would be to assess the level of BP accurately. To manage hypertension, limiting dietary intake, and individualizing dialysate sodium delivery would be the first steps. Antihypertensive drug therapies can effectively reduce BP and are needed by the vast majority of hemodialysis patients³⁴. Whether control of hypertension translates into better outcomes is not known, but collective evidence suggests that hypertension should be controlled in hemodialysis patients.

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