Blood Pressure Management in Hemodialysis Patients

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Dr. Van Buren is a general nephrologist and clinical researcher. His primary clinical interests are pre-dialysis management of chronic kidney disease, particularly diabetic nephropathy, as well as the comprehensive management of hemodialysis patients. He currently has funding through an NIDDK K23 award to study mechanisms of increased ambulatory blood pressure in patients with intradialytic hypertension. His long term research interest is to improve cardiovascular outcomes in hemodialysis patients through tailored fluid management and blood pressure control.

Purpose and Overview:
The purpose of this presentation is to provide Internal Medicine practitioners with an idea of the magnitude and clinical relevance of hypertension in hemodialysis patients. It will inform practitioners of the active changes that occur in blood pressure during and between hemodialysis treatments in these patients, as well the prognostic and diagnostic information from those changes. It will review the strategies utilized by nephrologists to manage hypertension including medications that all practitioners commonly prescribe.

Educational Objectives:
1. Identify the general prevalence of hypertension in hemodialysis patients
2. Be familiar with the pathophysiologic mechanisms responsible for hypertension in hemodialysis patients
3. Be familiar with various BP patterns exhibited during and between hemodialysis treatments and recognize the clinical significance of these patterns.
4. Be familiar with recent perspectives on the phenomenon of intradialytic hypertension
5. Become familiar with the available clinical trial data evaluating the role of pharmacologic antihypertensives in hemodialysis patients.

INTRODUCTION

The end-stage renal disease (ESRD) population continues to increase in the United States. Hypertension is one of the most common comorbidities in this patient population, and high blood pressure is strongly associated with cardiovascular morbidity and mortality. The increasing prevalence of ESRD in this country and the overwhelming prevalence of hypertension in these patients warrant the attention of all Internal Medicine physicians that will likely be involved in their care to any extent. The pathophysiology of hypertension is complex in these patients and involves extracellular volume overload in addition to disturbances in important physiologic pathways including the renin-angiotensin-aldosterone system and sympathetic nervous system. In addition to understanding the factors that make hypertension so common in these patients, it is useful to understand how the dialysis procedure itself and individual patient's response to hemodialysis may influence blood pressure, which is truly a moving target in these patients. The goal of this presentation is to 1) review the epidemiology and pathophysiology of hypertension in ESRD; 2) discuss intradialytic and interdialytic blood pressure patterns in hemodialysis patients, especially intradialytic hypertension and their associations with prognosis, and 3) review what is known about the role of pharmacologic antihypertensive therapy in hemodialysis patients.

EPIDEMIOLOGY

The ESRD Population In the United States

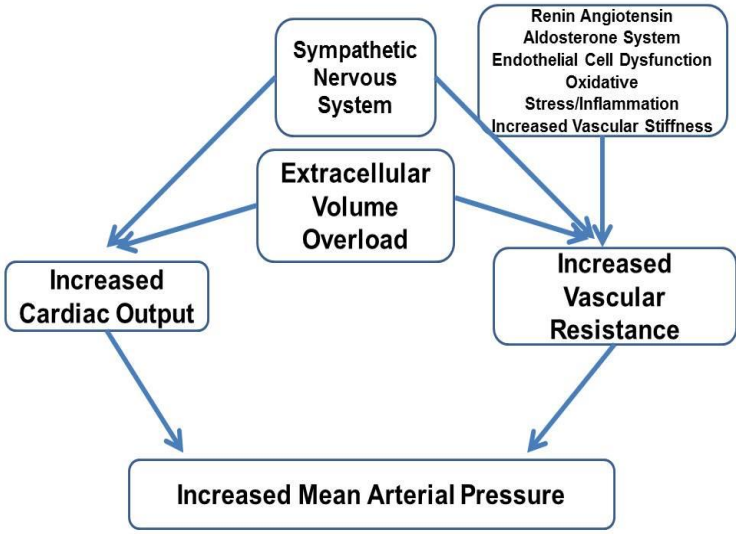
The most recent data from the United States Renal Data System indicates that 14% of the United States population has chronic kidney disease (CKD)[1]. The prognosis and severity of CKD varies within these patients, but 13.8% of patients with CKD are perceived to be at moderately high to very high risk of progression based on a very low baseline glomerular filtration rate, increased level of albuminuria, or a combination of both. Each year, there are more than 100,000 patients that progress to ESRD[1]. The prevalence of ESRD continues to increase with most recent estimates being more than 500,000. The vast majority of these patients will use maintenance hemodialysis as their modality of renal replacement therapy, as opposed to peritoneal dialysis or a kidney transplant. It is important for all physicians, regardless of specialty, to be aware of the unique complications and comorbidities among ESRD patients.

Hypertension and Kidney Disease

Recent National Health and Nutrition Examination Survey (NHANES) date indicates that hypertension is present in about 30% of the United States population, using the definition as a blood pressure of at least 140/90 mmHg or the use of an antihypertensive drug[2]. Hypertension is more common in individuals with CKD compared to those without, and prevalence increases with each progressive stage of CKD. By the time that a CKD patient has reached ESRD, the prevalence of hypertension can be as high as 90%[3]. Among patients with ESRD, there is little difference in the prevalence of hypertension between different age groups, races, ethnicity, or sex. The nearly universal prevalence of hypertension in these patients is due to the many risk factors that ESRD patients have for increased blood pressure even at the youngest of ages. These risk factors include both mechanisms that increase cardiac output and/or mechanisms that increase vascular resistance.

PATHOLOPHYSIOLOGY

Figure 1: Pathophysiology of Hypertension in ESRD

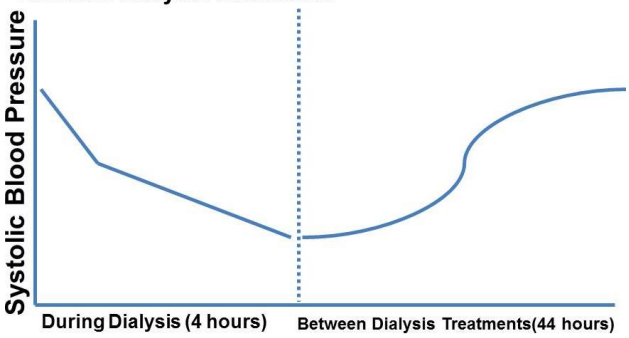


The numerous factors contributing to hypertension in ESRD patients are shown in **Figure 1**. End-stage renal disease patients have numerous reasons to have increased vascular resistance. This includes increased activity of the renin-angiotensin-aldosterone system, endothelial cell dysfunction, inflammation and oxidative stress, and increased arterial stiffness. Hemodialysis patients have also been shown to have increased sympathetic nervous system activity compared to healthy individuals. This increased sympathetic nervous activity appears to be more related to abnormal signaling from the diseased kidneys as opposed to some factor specifically related to uremia based on the reduction in activity following nephrectomy, but not following kidney transplantation[4,5].

Beyond these factors, extracellular volume overload is a critical component to hypertension in ESRD patients. Based on studies in anephric individuals, the expansion of extracellular volume causes an increase in blood pressure mediated by an increase in cardiac output[6]. If volume overload persists, there is reduction in cardiac output back down to the baseline, but the blood pressure remains elevated due to a delayed increase in vascular resistance. Hemodialysis patients are highly vulnerable to extracellular volume overload due to their limited urine output from failing kidneys. Sodium balance can only be achieved if these patients limit the amount of fluid gained from their diet to an amount that can safely be removed during the upcoming hemodialysis treatment.

One truly unique aspect of hypertension in hemodialysis patients is that blood pressure is continuously changing both during and between the hemodialysis treatments (**Figure 2**). Evaluation of one hemodialysis cohort's average blood pressure throughout a mid-week hemodialysis treatment showed that there is a two-slope decrease in blood pressure with an acute decrease in blood pressure during the first hour, with a blunted decrease during the remainder of the treatment[7]. These expected decreases in blood pressure occur in the context of 1) an acute reduction in extracellular osmolarity

Figure 2: Typical Blood Pressure Changes During And Between Dialysis Treatments



as diffuses out of a patient's blood during dialysis and 2) the decrease in intravascular blood volume caused by a prescribed volume of fluid removal (ultrafiltration) typically aimed to match the weight gain since the last dialysis treatment (interdialytic weight gain). There are numerous compensatory mechanisms which can minimize the hemodynamic changes induced by this reduction in blood volume, but the ultrafiltration rate remains a primary determinant of how steep the slope of blood pressure decline will be[7]. In short, faster ultrafiltration rates results in larger blood pressure drops during the dialysis treatment. During the interdialytic time period, the interval between consecutive dialysis treatments, there is typically a gradual increase in blood pressure from the end of one treatment until the beginning of the next treatment. Just as fluid removal can influence blood pressure changes during dialysis, the amount of weight gained between dialysis treatments can influence the blood pressure changes during the interdialytic period with larger weight gains resulting in faster increases in blood pressure.

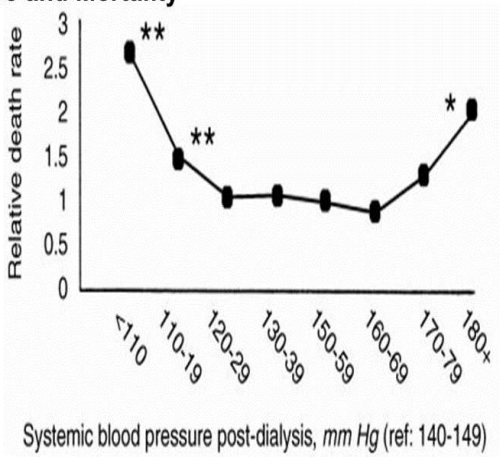
OUTCOMES RELATED TO HYPERTENSION

Due to the fact that blood pressure is frequently changing both during and between dialysis treatments, it is imperative to consider the consequences of high blood pressure at multiple points in time. Because nephrologist typically use hemodialysis-unit based measurements to make clinical decisions, these measurements had previously been the more frequently studied metric with regards to clinical outcomes. Just as in the general population, there is increasing interest in the prognosis of measurements obtained at home. There is also increasing interest in the prognosis of various blood pressure *patterns* during the hemodialysis treatment itself.

Hemodialysis Unit Measurements

When considering measurements obtained either immediately before or after dialysis, a U-shaped curve defines the relationship between blood pressure and mortality[8,9] (**Figure 3**). Among hypertensive patients, only those with the absolute highest blood pressure (either >200 mmHg before hemodialysis or >180 mmHg after dialysis) have increased mortality risk. The patients that have the overall highest mortality risk are those with low blood pressure. A likely explanation for the minimal mortality risk at moderate degrees of hypertension lies in the natural progression of cardiovascular disease.

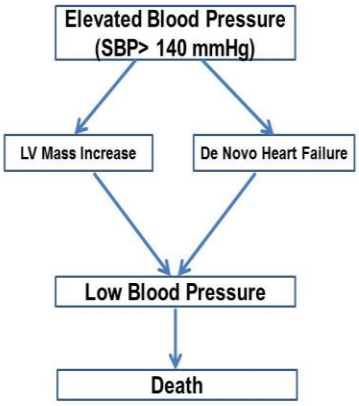
Figure 3: Relationship Between Post-Dialysis Blood Pressure and Mortality



Zager et al. *Kidney International* 1998; 54: 561

A prospective study in hemodialysis patients shows that for every 10 mmHg increment increase in mean arterial pressure, there is increasing left ventricular mass and an increased risk of de novo heart failure.[10] The risk for these outcomes was minimized around blood pressures of 140/90 mmHg. Once the heart undergoes these structural and functional changes, there is an expected decrease in both the cardiac output and blood pressure (**Figure 4**). The patients that develop heart failure after many years of hypertension have the highest mortality risk. Cardiovascular disease is the leading cause of death in ESRD patients, with the main individual causes including acute myocardial infarction, congestive heart failure, arrhythmia and sudden cardiac death. Despite the U-shaped curve from the large studies, it is still considered important to treat hypertensive hemodialysis patients and lower their blood pressure to levels that are associated with minimized risk for cardiovascular disease in general. The present guidelines set forth by the National Kidney Foundation recommend that clinicians aim to target a blood pressure of 140/90 mmHg before dialysis and 130/80 mmHg after dialysis.

Figure 4: Natural Progression of Cardiovascular Disease In Hypertensive Patients



Out of Hemodialysis Unit Measurements

The recognition that blood pressure is frequently changes at different points in time in hemodialysis patients has prompted the interest in looking at measurements obtained outside the hemodialysis unit. These measurements can include home measurements, where a patient measures his blood pressure at home 2-3 times per day with a standard blood pressure cuff and averages the results. An alternative is ambulatory blood pressure monitoring where an automated cuff is worn for the entirety of the interdialytic period. The cuff will automatically inflate every 30 minutes during the daytime and every hour at night, and the data is automatically recorded.

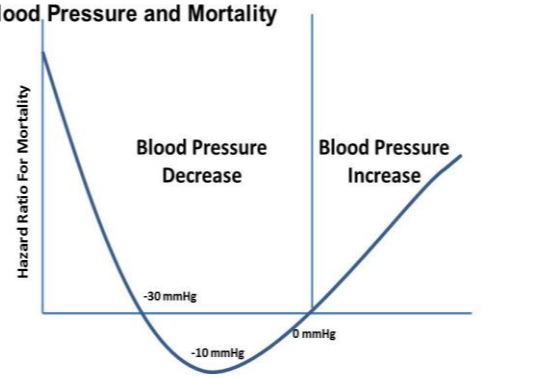
Blood pressure measurements obtained in the hemodialysis unit (including pre-dialysis, post-dialysis, the average of multiple intradialytic measurements) will all over-estimate blood pressure measured with an ambulatory monitor[11]. The post-dialysis measurement has the least amount of bias, and the pre-dialysis measurement has the most bias. The best precision is achieved by including as many intradialytic measurements as possible. Just as there are inherent differences in the measurements obtained in or out of the hemodialysis unit, there are also differences in the prognostic utility of such information. Compared to pre or post dialysis blood pressure measurements from the hemodialysis unit, those obtained with home or ambulatory blood pressure monitoring are better predictors of clinical endpoints including end organ damage such as left ventricular hypertrophy, as well as mortality[12,13]. While less convenient, ambulatory monitoring is considered superior to home blood pressure monitoring. It has become widely recognized that home and ambulatory blood pressure monitoring better assesses the overall blood pressure burden than hemodialysis unit measurements. However, implementation of these strategies may be

either too costly or not logistically possible for many patients. Ambulatory blood pressure monitoring is not yet widely implemented in clinical practice.

Intradialytic Blood Pressure Patterns

Without an ability to ascertain what is happening with blood pressure outside the unit, managing hypertension in hemodialysis patients remains a challenging task. There has been much interest recently into ways to better ascertain BP burden based on hemodialysis unit measurements, with a focus on intradialytic blood pressure *patterns*. It has become apparent that another U-shaped curve dealing with blood pressure and mortality is the one that describes the mortality risk of blood pressure change from pre to post dialysis (**Figure 5**). More specifically, compared to modest reductions in blood pressure from pre to post dialysis, those with either 30 mmHg decrease or *any* increase in systolic blood pressure have been associated with significantly increased mortality risk[14]. Increasing attention to intradialytic blood patterns has also generated interest into the specific pathophysiology explaining such patterns as well as interest in more specific management strategies for each pattern. Based on the natural tendency for blood pressure to decrease during the course of a dialysis treatment, the phenomenon of **intradialytic hypertension** is particularly intriguing.

Figure 5: Relationship Between Intradialytic Change In Blood Pressure and Mortality



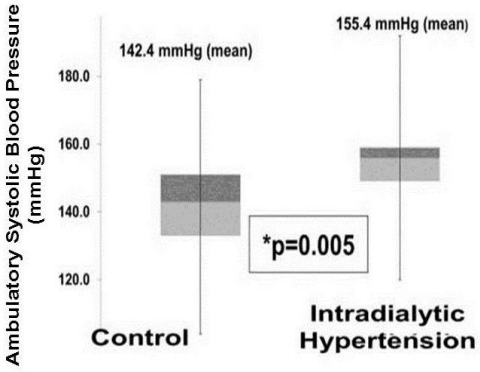
Intradialytic Hypertension

Intradialytic hypertension refers to an increase in blood pressure from pre to post-dialysis. While general fluctuations and variability in blood pressure can cause almost every hemodialysis patient to experience this intermittently, there is clearly a subset of hemodialysis patients that experience intradialytic hypertension on a frequent and recurrent basis[15]. While the overall prevalence will vary depending on the specific magnitude of blood pressure rise, it is estimated that about 15% of the hemodialysis population experience this regularly. Among hypertensive hemodialysis patients, those with intradialytic hypertension have some of the worst clinical outcomes. Numerous studies have replicated the findings that patients with intradialytic hypertension have increased hospitalization and mortality rates compared to hemodialysis patients with decreases in blood pressure during dialysis[16,17].

One of the earliest hypotheses was that extracellular volume overload was the underlying cause of intradialytic hypertension. This was largely based on a small, uncontrolled study looking at a group of patients with dilated cardiomyopathy that were prone to intradialytic hypertension. In these patients, it was shown that the initiation of fluid removal during dialysis led to an increase in cardiac output and blood pressure. As the patients then had more aggressive fluid removal, there was normalization of the blood pressure and reduction in the cardiac output. However, a case-control study with

a better design has since shown that there are no differences in cardiac output in patients with intradialytic hypertension and patients without increases in blood pressure[18]. In this study, the primary hemodynamic difference between the two groups was that patients with intradialytic hypertension had significant increases in vascular resistance from pre to post-dialysis. There is conflicting evidence what the origin of this vascular resistance increase can be, with many suggesting this is related to dynamic changes in endothelial cell derived vasoconstrictors and vasodilators such as endothelin-1 and nitric oxide[19].

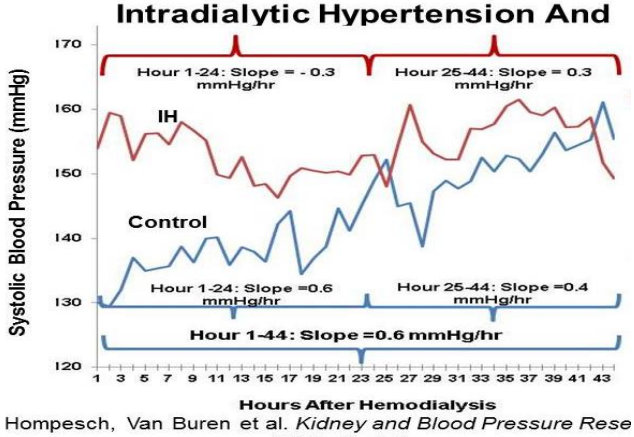
Figure 6: Comparison of Ambulatory Blood Pressure in Patients With Intradialytic Hypertension and Hemodialysis Controls



Van Buren et al. *Clin J Am Soc Nephrol* 2011; 6: 1684

While the pathophysiology of intradialytic hypertension remains somewhat unexplained, its association with mortality is becoming better understood. One case-control study showed that patients with intradialytic hypertension had significantly higher ambulatory blood pressure compared to hemodialysis controls[20] (**Figure 6**). It is possible the mortality risk of intradialytic hypertension is mainly related to a higher overall blood pressure burden in these patients. That case control study also showed that there was greater underlying endothelial cell dysfunction in the patients with intradialytic hypertension compared to controls[21]. This was determined based on a lower number of circulating endothelial progenitor cells measured before hemodialysis as well as lower flow-mediated vasodilation of the brachial artery measured on a non-dialysis day. Endothelial progenitor cells are bone-marrow derived cells that ultimately become endothelial cells. It is believed that these become deplete in the context of ongoing vascular injury. Flow mediated vasodilation measures the capacity of the brachial artery to dilate in response to shear stress. Impaired dilation is an indication of underlying endothelial cell dysfunction. While the higher ambulatory blood pressure and endothelial cell dysfunction were seen in the intradialytic hypertension patients, there was no evidence that there were significant differences in the intradialytic change in endothelin-1 between these patients and the controls.

Figure 7: Ambulatory BP Patterns Comparison Patients With Intradialytic Hypertension And



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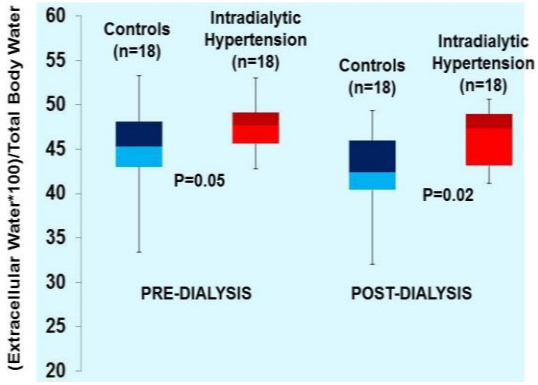
Further evaluation of the ambulatory blood pressure comparison showed that there was not only between-group differences in the average measurement, but there were also significant differences in the interdialytic patterns (**Figure 7**). Specifically, the controls demonstrated an expected gradual increase in blood pressure during the entire interdialytic period with an average increase in systolic blood pressure of 0.6 mm/Hg

(0.6 mmHg/hr for the first 24 hours, and 0.4 mmHg/hr for the remainder of the period)[22]. The patients with intradialytic hypertension demonstrated a decrease in blood pressure during the initial 24 hour period (-0.3 mmHg/hr), and then blood pressure increased for the remainder of the interval (0.3 mmHg/hr). The slope during the initial 24 hour period of the intradialytic hypertension patients was significantly different from their own slope during the remainder of the treatment as well as being different from the initial 24 hour slope in controls. The quantitative and qualitative differences between the patterns of these patients with controls suggest a form of hypertension that is mediated by some factor other than extracellular volume-dependent increases in blood pressure. This is further supported by the fact that there was no difference in interdialytic weight gain between the two groups during this case-control study. Current investigation in this area is focused on 1) obtaining more reliable measurements of extracellular volume in these patients with multifrequency bioimpedance spectroscopy, 2) establishing the inciting stimulus for intradialytic blood pressure increase, and 3) defining the relationship between changes in hemodynamics (cardiac index, vascular resistance index) and circulating vasoconstrictors (endothelin-1, angiotensin-II, asymmetric dimethylarginine) with the blood pressure changes during **and** between the dialysis treatments, where the overall blood pressure burden is highest. The preliminary data using multifrequency bioimpedance spectroscopy to measure the ratio of extracellular water to total body water indicates (**Figure 8, unpublished)** that patients with intradialytic hypertension are in fact more chronically volume overloaded than hemodialysis controls despite similar weight gain between treatments. The outcomes of the other aims remain underway. As discussed below, it is difficult to differentiate whether the chronic volume overload is a feature specifically associated with intradialytic hypertension or whether this is simply a finding common among all hemodialysis patients with high blood pressure at the end of dialysis.

Figure 8: Pre and Post Dialysis Extracellular/Total Body Water in Patients With Intradialytic Hypertension And Hemodialysis Controls



Increased Post Dialysis Blood Pressure

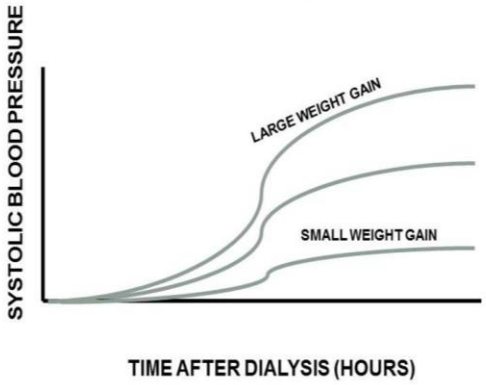
Regardless of the starting blood pressure or the amount of fluid removed during dialysis, there is increasing evidence that high post-dialysis blood pressure is a good indicator of chronic extracellular volume overload. Observational data shows that post dialysis blood pressure is higher in patients whose intravascular blood volume does not decrease much during dialysis compared to those with large decreases in intravascular blood volume [23]. Preservation of intravascular blood volume would be expected in patients who 1) had a small amount of prescribed ultrafiltration during dialysis or 2) had a larger amount of prescribed ultrafiltration during dialysis, but had rapid filling from the interstitial space into the intravascular space due to being chronically volume overloaded. In either case, it is evidence that more fluid removal could be considered in future treatments. A more recent cross sectional study using multifrequency

bioimpedance spectroscopy in 500 hemodialysis patients during a single treatment found that patients in the highest tertile of extracellular water to total body water measured after dialysis also had the highest systolic blood pressure after dialysis[24]. The emerging technologies to measure extracellular volume will provide even further guidance for blood pressure management in our hemodialysis patients.

Increased Pre-Dialysis Blood Pressure

The mortality risk of intradialytic hypertension was surprising to many people because such patients typically arrived to the dialysis unit with normal blood pressure. This contrasts from the presentation of most hemodialysis patients whose blood pressure is highest before dialysis. As discussed in the pathophysiology section, changes in extracellular volume can influence blood pressure during dialysis and between dialysis treatments. In most cases, high pre-dialysis blood pressure is an indication of acute extracellular volume expansion. There is a strong positive correlation between interdialytic weight gain and pre-dialysis blood pressure[25]. During the interdialytic period, patients who gain more weight have faster increases in blood pressure than patients who gain less weight (**Figure 9**). It can be difficult to determine whether there is underlying chronic extracellular volume overload in these patients as the excessive interdialytic weight gains prompt aggressive fluid removal during dialysis that can trigger significant hypotension during dialysis. Just as intradialytic hypertension is associated with increased mortality, so is the phenomenon of intradialytic hypotension where blood pressure plummets during the dialysis treatment (typically >30 mmHg decrease). While the topic of intradialytic hypotension is beyond the scope of this discussion, it is important to know that there is an independent association between the rate of fluid removal and mortality[26]. As discussed below, the first step in the management of a patient with high blood pressure before dialysis should be limitation of interdialytic weight gain.

Figure 9: Relationship Between Interdialytic Weight Gain and Blood Pressure Between Dialysis Treatments



GENERAL HYPERTENSION MANAGEMENT

Non-Pharmacologic Management

The multifactorial pathophysiology of hypertension in hemodialysis patients warrants a multifaceted approach to management. This will include dietary modifications, dialysis prescription modifications, and the use of pharmacologic agents. The first step in assessing a hypertensive hemodialysis patient should include evaluation of his extracellular volume status. While physical examination is notoriously unreliable, careful attention to the patient's blood pressure (before, after, and between treatments if available), weight gain, and intradialytic blood pressure patterns can provide additional clues. Available technologies such as multifrequency bioimpedance spectroscopy and on-line hematocrit monitoring are not routinely used in clinical practice, but there is hope

for more reliable non-invasive methods to measure extracellular volume to be integrated into dialysis care in the future.

The first intervention to address in a patient that appears to be extracellular volume overloaded is limitation of interdialytic sodium and fluid intake. Lower weight gains will result in lower pre dialysis blood pressure and less hemodynamic instability during dialysis. For patients that are considered to be extracellular volume overloaded after dialysis has taken place (either based on physical examination or blood pressure assessment), then additional fluid removal should be prescribed for the ensuing treatments. One randomized trial demonstrated that among hypertensive hemodialysis patients, removing small additional amounts of fluid each treatments (about 1% of body weight each week) resulted in a significant reduction in both post dialysis blood pressure and ambulatory blood pressure[27]. If this intervention cannot be tolerated, then either no further fluid removal is necessary or the patient should have more frequent or longer hemodialysis treatments so that the ultrafiltration rate is decreased. Observational studies and randomized trials evaluating different systemic delivery of hemodialysis show that increasing the overall duration a patient spends on dialysis (frequent daily dialysis, long nocturnal treatments) results in lower blood pressure. Unless the patient's blood pressure is dangerously elevated at home or at the dialysis unit, both limitation of interdialytic weight and consideration of further fluid removal should be considered prior to increasing or adding more antihypertensive medication.

Pharmacologic Antihypertensive Medications

While fluid management should be the initial priority in the management of a hypertensive hemodialysis patient, there is an inevitable role for the use of pharmacologic antihypertensive drugs. There is presently no randomized clinical trial that has been conducted that identifies the mortality benefit of one specific drug or class of drugs among a heterogeneous population of hemodialysis patients. There has also never been a clinical trial that demonstrates the benefit of a specific blood pressure target. There is meta-analysis evidence that the use of antihypertensive drugs in general is associated with reduced mortality in hemodialysis patients[28].

The National Kidney Foundation recommends initial treatment with Angiotensin Converting Enzyme (ACE) inhibitors, possibly due to early observational evidence of a mortality benefit from this class[29]. In this study, patients that had survived on dialysis for at least one year were followed to see if there was a difference in survival between patients that had been taking ACE inhibitors (6 month minimum) and those that had not. There was a significant reduction in mortality in the ACE inhibitor group that was largely due to a decrease in cardiovascular mortality. Since that study, the ACE inhibitor Fosinopril has been investigated in a placebo controlled randomized clinical trial[30]. The primary end point in this study was combination of fatal and non-fatal cardiovascular events. There was no difference in this outcome in the intention to treat analysis, but there was a trend towards benefit in the Fosinopril group in the per-protocol analysis. Acknowledged limitations of the study were an overall lower than predicted number of end points in both groups and greater comorbidity burden at baseline in the Fosinopril group. Because of these limitations, there remains interest in further studying the effects of ACE inhibitors and Angiotensin Receptor Blockers (ARB) in hemodialysis patients in larger studies. The results from studies looking at ARB are

mixed with some smaller randomized studies showing benefits compared to placebo for cardiovascular events[31,32]. In reconciling the small sample-size of many of the ARB studies, one meta-analysis failed to show a mortality benefit from ARB.

Beta-adrenergic receptor blockers have also been studied in hemodialysis patients. One randomized trial demonstrated a benefit of carvedilol in hemodialysis with congestive heart failure[33]. In this study, all patients had left ventricular systolic function <35%, and all patients were taking digoxin with the majority of these patients also receiving ACE inhibitors or ARB as well. The study showed decreased all-cause mortality, decreased cardiovascular mortality, and decreased hospitalizations in the patients randomized to carvedilol.

Another recent trial directly compared the beta blocker atenolol with Lisinopril[34]. In this trial, all patients had left ventricular hypertrophy and took the study drug three times a week. While the primary endpoint was change in left ventricular mass, the study was halted earlier due to increased cardiovascular events and hospitalizations in the Lisinopril group. At the time of study termination, there was no appreciable difference in left ventricular mass between these two groups.

In summary, antihypertensive medications should be used in patients whose blood pressure cannot be maintained with fluid management alone either due to non-adherence or a mechanistic resistance. There is not evidence that ACE inhibitors reduce mortality, but ACE inhibitors or ARB may reduce improve intermediate end points such as cardiovascular events. Beta blockers should be used in patients with congestive heart failure and/or coronary artery disease with there being clinical trial evidence supporting the former. A direct comparison of beta blockers and ACE inhibitors will likely be forthcoming in the future. Additional medications should be prescribed to patients as necessary using patient tolerance and side effect profile as the ultimate determinant of which drugs to use. It is not common that dialysis patients require numerous medications including some less frequently used in the general hypertensive population such as guanfacine and minoxidil. Although there is no evidence to support this, high doses of loop diuretics can be used to more easily achieve fluid balance in patients with some urine output remaining.

CONCLUSION

Knowledge of the mechanisms and treatment of hypertension is important to all Internal Medicine physicians due to the overwhelming prevalence of hypertension in these patients and the continuously growing ESRD population. The underlying pathophysiology is multifactorial, but extracellular volume overload is a critical component. Hypertension is associated with increased cardiovascular disease and indirectly related to mortality. The best methods of evaluating mortality risk continue to evolve, but there is growing interest in intradialytic blood pressure patterns such as intradialytic hypertension and in the information from the interdialytic period. These methods cannot only provide prognostic information, but also provide unique insight into some of the specific mechanisms at play. The management of hypertension requires aggressive attempts to achieve sodium balance, but will likely ultimately require medications with ACE inhibitors and beta blockers being at the top of the list.

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