Factors Affecting Blood Pressure Control in Hemodialysis

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Abstract

Background: Hypertension is poorly controlled in hemodialysis (HD). Extracellular fluid volume control, restriction of salt intake and antihypertensive therapy are needed to control blood pressure (BP) in this population. Research on patterns of antihypertensive use on BP has not been extensively studied in the chronic HD population.

Methods: A descriptive secondary correlational analysis of n = 118 chronic HD patients was conducted to determine the patterns of antihypertensive medication use and their relationship to BP.

Results: Participants were taking an average of three antihypertensive medications. Total number of antihypertensive medications was not correlated with BP. There were no differences in BPs in patients who took or did not take a specific antihypertensive drug class except for ace-inhibitors. Those participants who did take ace-inhibitors had significantly higher BPs.

Conclusions: Future studies examining antihypertensive class, optimal dosing and time of administration need to be conducted to determine the best hypertensive management intervention for chronic HD patients.

Keywords: Hypertensive management; Ace-inhibitors; Hemodialysis

Introduction

The estimated prevalence of hypertension in chronic Hemodialysis (HD) patients is 60 - 90% [1,2]. Hypertension in the chronic HD population is a major contributor to cardiovascular morbidity and mortality. There is a 20 fold greater incidence of cardiovascular mortality in the End Stage Renal Disease (ESRD) population compared to the general population without renal failure [3]. Systemic hypertension has been identified as a major risk factor for the progression of atherosclerosis, left ventricular hypertrophy, left ventricular dilation, heart failure and death [2,4,5]. According to Ritz and Koch, hypertension is the single most important predictor of coronary artery disease in uremic patients, even more so than cigarette smoking and hypertriglyceridemia [3]. Agarwal and Sinha demonstrated that control of Blood Pressure (BP) in HD patients regresses left ventricular hypertrophy and improves cardiovascular morbidity and mortality [6]. According to National Kidney Foundation Kidney Diseases Outcomes Quality Initiative guidelines (NKF KDOQI) (2005), the goal for predialysis and post dialysis blood pressure should be <140/90 mm Hg and <130/80 mm Hg respectively [7].

Despite advances in BP management in the general population, hypertension remains a challenge to control in the chronic HD population. In a study of 2,535 clinically stable adult HD patients, 86% were found to be hypertensive [2]. Within this hypertensive group, only 30% had their BP under adequate control, 58% were inadequately treated, and 12% were not treated at all [2]. Rocco et al. found similar results in a sample of 1,238 maintenance HD patients, where less than 30% had BPs that were considered normotensive by the Joint National Committee (JNC) VI standards [8].

The pathophysiology of hypertension in End Stage Renal Disease (ESRD) is complicated and multifactorial. Literature indicates that the major reason for hypertension in this population is fluid overload secondary to fluid and sodium retention [9-11]. Patients with ESRD have an inability to excrete sodium and water by the kidneys which results in increased extracellular volume, increased cardiac output and increased BP. Non adherence to HD regimens by missing HD treatments or cutting total time on HD may also result in increased extracellular fluid volume.

Extracellular fluid volume control, achievement of dry weight and restriction of sodium intake are the initial treatments for BP control. In addition to fluid and sodium restriction, pharmacologic interventions are also frequently needed to control BP in HD. According to NKF KDOQI guidelines, the first line agents to treat hypertension in HD patients should be renin angiotensin aldosterone system (RAAS) blocking agents: ace inhibitor or angiotensin II receptor blockers [7]. Because hypertension is so difficult to control in the HD population, additional agents such as beta blockers, calcium channel blockers and alpha blockers are frequently needed. Coexistent comorbidities should be considered when choosing further antihypertensives [7].

Although there is ample literature on the effect of Interdialytic Weight Gain (IDWG) on blood pressure, there is minimal research on the patterns of antihypertensive medication use and the effect of various antihypertensive classes on BP outcomes in the HD population. The major purpose of this secondary data analysis was to evaluate the patterns of antihypertensive use in a sample of HD patients and their effect on blood pressure. The secondary aim of the study was to examine the relationships between IDWG, total missed HD treatments, antihypertensive medication class, and total number of antihypertensive medications, medication adherence and BP.

Methods

Design

The data from this descriptive comparative study came from a secondary analysis of cases (n = 118) available from a Randomized Controlled Trial (RCT) aimed to test the effectiveness of a BP self care

regulation intervention on blood pressure. Details of the study have been published [12].

Study sample

A convenience sample was drawn from six outpatient HD units in Michigan. The studies were approved by the HIC at Wayne State University and each of the study sites. Patients were considered eligible for the study if they were (a) > 18 years, (b) had a four week average pre HD BP > 150 mm Hg or diastolic BP > 90 mm Hg and (c) read and spoke English. Exclusion criteria included: (a) on HD less than 6 months; (b) illicit drug use history; (d) history of mental illnessor; (e) lack of orientation to person, time or place; (f) major health problem such as terminal cancer or HIV; and (g) missing greater than two HD treatments over a four week period. If determined eligible, the medical director and/or nurse manager of each HD unit initially contacted patients. If patients indicated interest in the study they were referred to the PI. If the potential participant was interested in participating in the study, they were asked to sign a written consent.

Procedure

BP and IDWG data were collected from a chart review of the HD flow sheets at baseline and 12 weeks after initiation of the study. Baseline BP was calculated as average 4 week BP before initiation of the study and was calculated by averaging three weekly pre HD BPs for 4 weeks. Average twelve week BP was calculated by averaging 3 weekly pre HD BPs for 12 weeks. IDWG was calculated by subtracting the participant's previous post HD weight from their subsequent pre HD weight. Average baseline IDWG was calculated as average 4 week IDWG before initiation of the study. Three weekly IDWGs were calculated and averaged over 12 weeks.

Information on total number and class of antihypertensive medications were collected from patient charts and verified verbally by patient. Total number of missed HD treatments was calculated as total number of missed HD treatments over 12 weeks. Demographic data (age, sex, race, educational level and income) were assessed and documented from patient charts at baseline. Medication adherence was measured using the Morisky Scale [13]. The Morisky scale has four items with dichotomous (yes/no) response options. The sum of yes responses provides atotal score of nonadherence. This tool has been validated and found to be reliable in a number of studies [13,14]. Medication adherence was measured at baseline and 12 weeks.

Data management

All data was collected from patient charts and dialysis flow sheet by the principal investigator (PI). Data was coded and entered into SPSS 17.0 by the PI. Descriptive statistics were conducted on all study variables. Pearson's correlations statistics were conducted to examine the association between missed HD treatments, fluid gains (IDWG), total number of antihypertensive medications, medication adherence scores and BP. Independent t-tests were conducted to compare differences in BP between those who did and did not take a particular antihypertensive drug class.

Results

The sample consisted of 118 participants. The average mean age of the sample was 59.7 years (SD = 15.9), with a range from 19 to 91 years. The sample was represented by 60 (51%) men and 58 (49%) women. The race composition of the sample consisted of 101 (86%) African Americans, 14 Caucasians (12%), and 3 (2.5%) Middle eastern.

The average years of education for the sample was 12.43 years (SD = 2.3) with a range of 3 to 20 years. The majority of the sample was unemployed (n = 99, 83.9%) with 58 (49.2%) participants earning a total yearly household income of less than $10,000.Sixty three percent of the sample were not married and 44 (37%) were married or living with a partner. Fifty percent of the sample had diabetes, 33% of the sample had pre-existing atherosclerotic heart disease and 25% of the sample had congestive heart failure.

The average systolic BP (SBP) at baseline was 163 mm Hg (SD = 12.4) and 158.5 mm Hg (SD = 12.5) at 12 weeks. Of the 118 patients enrolled in the study, the majority, 65 (55%) had stage 2 systolic hypertension (SBP > 160 mmHg); 53 (45%) had Stage 1 hypertension (SBP 140-159 mm Hg).The baseline average diastolic BP (DBP) for the sample was 87. 3 mm Hg (SD = 10.2) and 85.3 mmHg (SD = 10.4) at 12 weeks. In terms of diastolic hypertension, 34 (29%) had stage 1 diastolic hypertension (DBP 90-99 mm Hg) and 14 (12%) had stage 2 diastolic hypertension (DBP > 100 mmHg). Seventy patients (59%) did not have diastolic hypertension.

Average fluid gains were 2.46 kg (SD = 1.0) at baseline with a range of .1 to 6.3 kg and 2.47 kg (SD = 1.0) at 12 weeks with a range of (.24 to 6.3 kg). Total average missed HD treatments was 1.1 (SD = 1.4) with a range of 0 to 6 missed HD treatments. The majority of the participants were taking antihypertensives (n = 116, 96.6%).Two participants (1.7%) were not taking any antihypertensives. Table 1 identifies the frequencies of antihypertensives taken amongst the sample. In order of frequency, beta blockers were the most frequently used antihypertensive (n = 94, 79.7%), followed by calcium channel blockers (n = 65, 55.1%). Ace inhibitors were used by 57 (49.2%) participants of the sample and 48 (41%) participants were taking alpha blockers. Twenty five (21%) participants of the sample were taking angiotensin receptor blockers. Diuretics were only used by 13 (11%) of the sample.

Table 2 identifies the total number of antihypertensive medications taken by the sample. Sixty four participants (54%) of the sample were taking three or more antihypertensives. The average number of antihypertensives taken by the sample was 2.6 (SD = 1.1) with a range of zero to six. Interestingly total number of reported antihypertensives was not significantly related to baseline systolic BP (r = 0.03, p = 0.72) and baseline diastolic BP (r = 0.10, p = 0.27) or 12 week systolic BP (r = 0.09, p = 0.35) and diastolic BP (r = 0.73, p = 0.43). Total number of antihypertensives was not significantly related to medication

Variable	Frequency (%) (n = 118)
Beta-Blockers	94 (79.7)
Calcium Channel Blockers	65 (55)
Ace inhibitors	57 (49.2)
Alpha Blockers	48(41)
Angiotensin Receptor Blockers	25 (21)
Diuretics	13 (11)

Table 1: Frequency Distributions – Blood Pressure Medications.

Number of BP Medications	Frequency (%) (n = 118)
0	2(1.7)
1	20(16.9)
2	32(27.1)
3	45(38.1)
4	12(10.2)
5	6(5.1)
6	1(.8)

Table 2: Frequency Distribution of Number of BP Medications.

nonadherence scores at baseline($r = 0.05$, $p = 0.58$) or 12 weeks ($r = 0.03$, $p = 0.76$).

In this study, IDWG was not significantly related to baseline systolic BP ($r = 0.11$, $p = 0.24$) or 12 week systolic BP ($r = 0.09$, $p = 0.32$). However, IDWG was related to baseline diastolic BP ($r = 0.22$, $p = 0.02$) and average 12 week diastolic BP ($r = 0.20$, $p = 0.03$). Total number of antihypertensives was not significantly related to baseline IDWG ($r = 0.01$, $p = 0.96$) or 12 week IDWG ($r = 0.03$, $p = 0.72$). Total number of missed HD treatments was significantly correlated with baseline IDWG ($r = 0.23$, $p = 0.01$) and 12 week average IDWG ($r = 0.26$, $p = 0.004$). In addition, total number of missed HD treatments was correlated with baseline diastolic BP ($r = 0.37$, $p = 0.00$), 12 week systolic BP ($r = 0.32$, $p = 0.00$) and 12 week diastolic BP ($r = 0.45$, $p = 0.00$).

There was no significant effect of antihypertensive class on BP except for ace-inhibitors. At baseline, patients taking ace-inhibitors were found to have significantly higher systolic BPs ($M = 166$ mm Hg, $SD = 13.8$) ($t(116) = -2.1$, $p = 0.036$) compared to those who did not take ace-inhibitors ($M = 161$ mm Hg, $SD = 10.2$). Those who took ace inhibitors also had significantly higher systolic BPs ($M = 161$, $SD = 13.2$) at 12 weeks $t(116) = -2.3$, $p = 0.025$) compared to those who did not take ace-inhibitors ($M = 156$ mm Hg, $SD = 11.3$). Twelve week diastolic BPs weeks were also significantly higher in those who took ace-inhibitors ($M = 87.6$ mmHg, $SD = 10.7$) compared to those who did not ($M = 83$ mm Hg, $SD = 1.2$)($t = -2.4$, $p = 0.02$).

Independent t-tests were conducted to determine if there were differences in those participants taking ace-inhibitors or alpha angiotensin receptor blockers and total number of antihypertensives. Participants taking ace-inhibitors were taking significantly more antihypertensive medications ($M = 3$ BP meds, $SD = 1.2$) ($t(116) = 4.3$, $p = .00$) compared to those who were not taking ace-inhibitors ($M = 2.2$ BP meds, $SD = .94$). Similarly, those taking angiotensin receptor blockers were also on significantly more antihypertensive medications ($M = 3.1$ BP meds, $SD = 1.2$) ($t(116) = 2.3$, $p = 0.01$) than those not taking angiotensin receptor blockers ($M = 2.4$ BP meds, $SD = 1.1$).

Discussion

A number of interesting findings were found in this study. This study confirms poor BP control in chronic HD patients. Systolic hypertension was much more prevalent in this sample than diastolic hypertension. The majority of patients were on three or more antihypertensives. Despite being on a number of antihypertensives, most of the participants did not have adequate BP control. The most frequently prescribed antihypertensive agent were beta blockers followed by calcium channel blockers and ace inhibitors. Total number of antihypertensives was not related to BP or medication adherence. IDWG was significantly related to diastolic BP at baseline and 12 weeks. Total missed HD treatments were significantly correlated to IDWG and diastolic BP. Patients who took ace inhibitors or angiotensin receptor blockers had significantly higher BPs than those who did not.

The choice of antihypertensives used in this sample does not follow the recommendations outlined by the National Kidney Foundation KDOQI guidelines for treatment of hypertension in HD [7]. According to the guidelines, drugs that inhibit the renin-angiotensin system such as ace-inhibitors or angiotensin II receptor blockers should be the preferred drug of choice in this population. Only 82 patients (68%) were taking an ace inhibitor or angiotensin II receptor blocker compared to 94 patients (79.7%) who were taking a beta blocker or 65 patients (55%) who were taking a calcium channel blocker. Possible

explanations for this finding may be that antihypertensive agents are not being prescribed as per NKF KDOQI guidelines. Ace inhibitors or angiotensin blockers may have been used as third line antihypertensive agents to help improve BP control. Further, exploration of possible reasons why NKF KDOQI guidelines for hypertension in HD are not being followed needs to be conducted.

Interestingly, the choice of antihypertensive agent did not influence BP response. There was no significant difference in BP between those who took and did not take a specific drug class except for ace-inhibitors. This study found that BPs were significantly higher in patients taking ace-inhibitors or angiotensin receptor blockers compared to those patients not taking these drugs. Since antihypertensive dosages were not recorded in this study, it was difficult to determine whether the study participants had higher BPs because they were not on maximum doses of ace-inhibitors or angiotensin II receptor blockers. Another explanation could be that many of ace-inhibitors are removed through HD which may result in higher BPs. Perhaps the patients on ace-inhibitors had higher BPs that required more antihypertensives to control. Another possible explanation is that ace inhibitors and angiotensin receptor blockers may not be as effective as other antihypertensive drugs in controlling BP in this population.

A possible explanation for poor BP control in this population is nonadherence to antihypertensive medications secondary to the complexity of the medication regimen. In this study, total number of antihypertensive medications was not found to be related to medication adherence scores. The Morisky tool used to measure medication adherence was a self-report tool which may have resulted in social desirability bias and affected validity of findings. Future studies incorporating other methods of measuring medication adherence should be conducted to confirm these findings.

This study also confirms the effect of excessive IDWG on increased diastolic BPs. Methods to enhance fluid and salt restrictions and adherence to HD regimens still need to be reinforced with chronic HD patients. However, in this study, a number of participants had high BPs despite having low IDWGs. Thus, we need to consider that overhydration is not the only reason why many HD patients are hypertensive. These findings have been validated in the literature. Wabel et al. conducted a study of 500 HD patients and measured pre dialysis systolic BP and fluid status by bioimpedance [15]. They found that only 15% of the sample was overhydrated and had hypertension. Interestingly, 13% of the sample had hypertension despite underhydration and 10% had overhydration despite normal or low BP.

Strengths of the study include that it was a prospective study that measured variables related to BP at two time periods, baseline and 12 weeks. The study also examined the use of antihypertensives in a chronic HD population which has not been extensively studied in the literature. Limitations of the study included sample composition with 86% of the sample being African American. This is not reflective of the racial composition of the general US HD population which is approximately 42% African American. Future studies need to be conducted that use samples representative of the US HD population to further validate the findings in this study. Other limitations included lack of data related to the variable of length of time on HD and not recording dose or timing of antihypertensives in order to determine whether these variables had an effect on BP. The Morisky tool used to measure medication adherence may have been subject to reporter bias and additional methods such as pill counts, prescription refills or electronic monitoring should be used in the future to increase reliability and validity of findings.

In conclusion, this study confirms that hypertension is still poorly controlled in chronic hemodialysis patients. Despite being on multiple antihypertensive medications and having recommended average IDWG, the majority of patients in this study still had poor BP control. This study also indicates that patterns of antihypertensive use in this sample do not follow recommended NKF KDOQI guidelines. Future studies need to be conducted to determine potential reasons why guidelines are not being followed. Further studies need to be conducted to determine best combination of antihypertensive medications and optimal dosing (dose and time of administration) in order to improve BP control in HD patients.

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