



Hypertension on Dialysis Patients: Influence Factors and Management

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ABSTRACT

Background: Hypertension remains prevalent and challenging to manage in patients with chronic kidney disease, even with renal replacement therapy. This phenomenon arises from a variety of components that contribute to and create an intricate process of interaction, which can impact the regulation of blood pressure in patients undergoing dialysis. The main goal of this overview is to find the influence factor of blood pressure in dialysis patients and investigate ways to better control their blood pressure by incorporating these factors.

Methods: The literature searches using online databases such as PubMed and Google Scholar.

Results: After doing an online search, we found 32 articles were relevant to this review topic.

Discussion: There are additional elements that contribute to hypertension in dialysis patients, including excessive volume, heightened arterial rigidity, stimulation of the renin-angiotensin-aldosterone system, sleep apnea, activation of the sympathetic nervous system, and the administration of recombinant erythropoietin.

Conclusion: Enhanced comprehension of the numerous variables at issue can effectively enhance blood pressure regulation in this group of individuals.

Keywords: Chronic Kidney Disease, Dialysis, Hypertension, Management, Influence Factors

ABSTRAK

Latar Belakang: Hipertensi merupakan hal yang umum dan menantang untuk ditangani pada pasien dengan penyakit ginjal kronis, bahkan pada mereka dengan terapi pengganti ginjal. Fenomena ini disebabkan terdapat berbagai komponen yang berkontribusi dan menimbulkan proses interaksi yang rumit, yang dapat berdampak pada pengaturan tekanan darah pada pasien yang menjalani dialisis. Tujuan utama dari tinjauan mendalam ini adalah untuk menemukan penyebab tekanan darah tinggi pada pasien dialisis dan mencari cara untuk mengontrol tekanan darah dengan lebih baik dengan mempertimbangkan faktor-faktor tersebut.

Metode: Setelah melakukan pencarian online, ditemukan 32 artikel yang relevan dengan

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topik.

Hasil: Terdapat berbagai faktor yang dapat mempengaruhi terjadinya hipertensi pada pasien dialisis meliputi kelebihan volume, kekakuan arteri, stimulasi system renin-angiotensin-aldosteron, sleep apnea, aktivasi system simpatis dan pemberian eritropoietin.

Kesimpulan: Peningkatan pemahaman tentang berbagai variabel yang menjadi permasalahan ini dapat secara efektif meningkatkan regulasi tekanan darah pada kelompok individu ini.

Kata Kunci: Penyakit Ginjal Kronis, Dialisis, Hipertensi, Manajemen, Faktor-faktor yang mempengaruhi

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1 Introduction

The leading cause of chronic kidney disease (CKD) is high blood pressure [1]. One notable aspect of CKD patients' treatment is that, even after receiving renal replacement therapy, such as hemodialysis (HD) or peritoneal dialysis (PD), hypertension remains a concern that needs to be taken into account. Poor survival rates and an increase in cardiovascular events are directly linked to elevated blood pressure [2].

Hypertension, defined as blood pressure over 140/90 mmHg, is frequently observed in patients who get regular hemodialysis, with a prevalence ranging from 50% to 60%. The issues faced by peritoneal dialysis patients are relatively similar, with a considerable variation in the prevalence rates of hypertension, ranging from 30% to over 80%.[2] The observed discrepancy could be attributed to varying approaches to establishing hypertension. Research conducted in the United States indicates that the incidence of hypertension remains elevated, ranging from 30% to 50%, even after undergoing treatment for hypertension [2,3].

The Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines from 2005 recommended a predialysis BP target of <140/90 mm Hg and a post-dialysis BP of <130/80 mm Hg. In Canada and Japan, guidelines have recommended a predialysis BP of <140/90 mm Hg. The UK Renal Association Standards Committee has advised a predialysis blood pressure target of <140/90 mm Hg and a post-dialysis target of <130/80 mm Hg. However, an audit conducted on 11 hemodialysis centers in the Greater London area, following these guidelines, revealed that only 26% of the total 2630 patients were able to achieve both blood pressure targets [1,4,5].

Hypertension is a contributing factor to mortality in patients with HD. Prior observational research has indicated that each 10 mmHg rise in systolic blood pressure during dialysis has an indirect correlation with a 6% increase in the hazard ratio for mortality [6]. Hypertension is a significant factor contributing to the elevated occurrence of coronary artery disease and left ventricular hypertrophy, which is the primary cause of mortality in individuals with chronic kidney disease. The occurrence of left ventricular hypertrophy (LVH) rises progressively with the

advancement of chronic kidney disease (CKD), peaking at 75% with the commencement of dialysis. Aside from anemia, hypertension is another risk factor that can be modified to lower the risk of death [7-9].

In dialysis patients, sodium and volume overload are the main causes of hypertension. Hence, the primary strategies adopted to attain blood pressure control involve nonpharmacological measures, including limiting sodium consumption, enhancing sodium elimination via dialysis, and establishing the appropriate dry weight. The therapy approach poses significant challenges due to various factors, including the limited duration of dialysis, patients not following the dialysis schedule, failure to adhere to sodium restrictions, and elevated sodium levels during dialysis caused by the use of high-sodium dialysate, all of which can impede the attainment of the desired dry weight. Despite implementing rigorous volume management strategies, hypertension continues to be inadequately regulated. Furthermore, there are additional elements that contribute to this phenomenon, including heightened arterial rigidity, stimulation of the renin-angiotensin-aldosterone system, sleep apnea, activation of the sympathetic nervous system, and the administration of recombinant erythropoietin [10,11].

Due to the several factors elucidated earlier, managing hypertension in dialysis patients appears to be challenging. Studying hypertension in dialysis patients is crucial, encompassing the cause variables, and treatment options, including both non-pharmacological and pharmaceutical approaches. This comprehensive analysis aims to identify the factors contributing to hypertension in dialysis patients and explore strategies to incorporate these aspects to optimize blood pressure management.

2 Methods

This was a narrative review of the influence factors and management of hypertension in dialysis patients. We do the literature searches using online databases such as PubMed, and Google Scholar. Published literature relating to “Hypertension in Dialysis” “Factor” and “Management” was obtained using the keywords “Hypertension in Dialysis”, and “Hypertension in Hemodialysis”, in association with “Factors” “Treatment” and “Management”. The articles must be in English and published in 10 years (2014 until 2023). Studies in non-English language and performed on animals were excluded from this review. The selected articles were carefully reviewed and analyzed to extract essential insights about the topic under discussion.

3 Results

Table 1 Total number of articles applying inclusion criteria

Online Database	Keyword	Number of Result
PubMed	Hypertension in Dialysis	1035
	Hypertension in Hemodialysis	10
	Hypertension in Dialysis, Factors	341
	Hypertension in Dialysis, Treatment	510
	Hypertension in Dialysis, Management	310
Google Scholar	Hypertension in Dialysis	815
	Hypertension in Hemodialysis	1090
	Hypertension in Dialysis, Factors	676
	Hypertension in Dialysis, Treatment	734
	Hypertension in Dialysis, Management	654

After doing an online search on PubMed and Google Scholar. We found 32 articles were relevant to this review topic. The articles were reviewed and analyzed to extract essential insights about the topic under discussion.

4 Discussion

4.1 Influencing Factors of Dialysis Patients' Blood Pressure

Excessive intravascular volume

The scientific explanation of hypertension in dialysis patients is complex and multifactorial. Elevated blood pressure in dialysis patients is mostly attributed to increased cardiac output, peripheral vascular resistance, or a combination of both. Excessive intravascular volume is a primary pathogenic component contributing to hypertension in dialysis patients. This expansion of extracellular volume is particularly prevalent in individuals with end-stage renal hypertension. Compared to individuals with normal blood pressure, hypertensive hemodialysis patients experience an increase in total body water. By eliminating surplus bodily fluid and attaining the “dry weight” through a slower and more frequent dialysis process, blood pressure can be enhanced in around 90% of patients [10,11].

Reports indicate that normalizing the volume of fluid outside the cells can enhance the circadian rhythm of blood pressure. Sodium and volume overload may contribute to persistent hypertension in patients who do not respond to intense ultrafiltration. Recent studies conducted by Wiig, Luft, and Titze have uncovered the existence of an unidentified sodium storage mechanism that is associated with glycosaminoglycan in the skin. [12] This mechanism serves as a protective barrier against external sodium. The capacity of this compartment is approximately 180-190 milliequivalents per liter. Regrettably, these reservoirs of sodium might be discharged into the bloodstream, leading to hypervolemia and oxidative stress, or triggering the activation of cellular pathways associated with tissue fibrosis [13]. In persons undergoing hemodialysis, there is an increase in salt and water content in the skin and muscles, but the levels of vascular endothelial

growth factor (VEGF) are decreased compared to those of normal individuals. These changes may play a role in the development of hypertension [4,14].

Role of Vascular Endothelial Growth Factor

Vascular endothelial growth factor (VEGF) was identified as a factor with the ability to stimulate the permeability of endothelial cells [14] and the formation of new blood vessels (angiogenesis) [15]. Currently, a total of seven members belonging to the VEGF family have been discovered. These include VEGF-A, VEGF-B, VEGF-C, VEGF-D, and VEGF-E, as well as placental growth factors 1 and 2. Nitric oxide directly influences the regulation of pressure natriuresis and tubuloglomerular feedback. Inhibiting VEGF may lead to an impairment of the usual functioning of endothelial nitric oxide synthase, resulting in salt retention. Kim et al. conducted an assessment of the levels of VEGF-C in the blood and urine of patients at different stages of chronic kidney disease (CKD), including those undergoing regular hemodialysis treatment [16]. The researchers postulated that there would be a correlation between the alteration in serum VEGF-C levels and the rise in blood pressure. In patients with chronic kidney disease (CKD), the levels of VEGF-C in the blood were much lower compared to healthy individuals. However, CKD patients had increased amounts of VEGF-C in their urine. VEGF-C levels were reduced in hemodialysis patients, however, blood pressure did not accurately correspond to the alterations in VEGF-C concentration. Kim et al. hypothesized that serum levels of VEGF-C could potentially rise in hypertensive CKD patients due to its association with salt-sensitive hypertension, and the hypertension observed in CKD patients may be connected to an increase in blood volume [14,16].

Renin-Angiotensin-Aldosterone System

The increased secretion of renin plays a significant role in the development of hypertension in dialysis patients, affecting their volume and salt levels. Activation of the renin-angiotensin-aldosterone pathway is a well-established occurrence in renal failure patients receiving dialysis. This leads to renin-dependent hypertension that is resistant to dialysis. Furthermore, secondary hyperaldosteronism exacerbates hypertension by elevating salt concentration, leading to potential harm to the kidneys, heart, and blood vessels [4,17].

Arterial Stiffness

A common problem seen in dialysis patients is increased arterial stiffness. This is mostly because their bodies are not breaking down calcium and phosphorus properly, which causes vascular calcification. Arterial stiffness in dialysis patients is evaluated by measuring aortic pulse wave velocity (PWV), which is strongly associated with elevated interdialytic blood pressure. [4] In a small observational study of 20 people on hemodialysis, lowering the calcium level in the dialysate from 1.75mmol/L to 1.5mmol/L led to improvements in both PWV and blood calcification markers [18]. The PWV is higher after a three-day break in the intradialytic process compared to a two-day break [19].

Autonomic Nervous System

Since the autonomic nervous system is heavily involved in modulating the intrinsic circadian fluctuation in blood pressure, SNS overactivity—a trait of patients with impaired renal function—could be a contributing factor [20]. The sympathetic nerve discharge in dialysis patients is 2.5 times greater compared to that of individuals without dialysis [2]. This increase in discharge is not associated with plasma noradrenaline concentrations or renin activity. Sympathetic nerve activation is caused by excess fluid that exceeds 6% of body weight, and it is believed that ACE-I can diminish this excessive sympathetic activity [4]. A study by Quarti-Trevano et al evaluated carotid and cardiopulmonary reflex responses in uremic patients before and after acute hemodialysis procedure. This study showed that after just one session of hemodialysis, the carotid baroreceptors' ability to control heart rate was greatly enhanced, and the vascular and humoral reactions to cardiopulmonary receptor deactivation were greatly enhanced. Autonomic responses may also be changed by the type of dialysis method used. Possibly this is the case for nighttime hemodialysis, which has been shown to lower plasma norepinephrine levels, raise endothelium-dependent vasodilatation, improve baroreflex sensitivity, and bring blood pressure back to normal in hypertensive patients with end-stage renal disease [21].

Asymmetric methylarginine

Patients with chronic renal failure also have impaired endothelial vasodilation due to uremia and nitric oxide insufficiency, which subsequently causes hypertension during hemodialysis and peritoneal dialysis. Asymmetric methylarginine (ADMA), which builds up in people with chronic kidney disease (CKD), especially those who have problems related to atherosclerosis, stops the production of nitric oxide [4,22].

Erythropoietin

Twenty to thirty percent of people with chronic kidney disease can get high blood pressure from taking the normal dose of human erythropoietin. The correction of anemia can lead to an increase in red blood cell mass, which in turn raises the overall viscosity of the blood and the workload on the heart, contributing to the development of hypertension. However, it is important to note that an increase in blood pressure can occur even before there is an increase in the proportion of red blood cells in the blood (hematocrit). Additional variables contributing to erythropoietin-induced hypertension include the release of endothelin, malfunction of the cells lining the blood vessels, pre-existing high blood pressure, elevated levels of calcium in the cytoplasm of the smooth muscle cells in the blood vessels, reduced production of nitric oxide, and early correction of anemia. A study by Li et al. on hemodialysis patients showed that each 1-unit SD higher in log (endothelin-1) was associated with a 1.46-fold increased risk of cardiovascular death [23]. According to Chang et al., erythropoietin causes smooth muscle cells to take in more calcium, which narrows blood vessels [24]. Erythropoietin also has an anti-natriuretic effect, which means it changes the

way sodium is flushed out of the body, which can cause high blood pressure [25]. Angiotensin II is what makes this anti-natriuretic effect of erythropoietin work. Sun et al. discovered that people with a certain allele of the angiotensinogen gene are more likely to get high blood pressure when they are treated with erythropoietin [26]. This means that angiotensin is a key part of how erythropoietin raises blood pressure, and variations in the angiotensinogen gene can affect the development of high blood pressure. Furthermore, higher doses of human erythropoietin, higher goal hemoglobin levels, and the type of dialysis used were all linked to higher blood pressure responses.

Sleep Apnea

Sleep apnea is also highly prevalent in CKD patients [27] and can be associated with fluid excess. The presence of low oxygen levels during sleep in individuals with sleep apnea is linked to elevated nighttime systolic blood pressure, increased thickness of the left ventricular wall, and the development of resistant hypertension. The obstructive apnea-hypopnea index is dramatically decreased during hemodialysis because of the reduction in fluid excess [28].

Secondary Hyperparathyroidism

Secondary hyperparathyroidism in individuals with chronic kidney disease (CKD) leads to hypertension by facilitating the influx of calcium into the smooth muscle cells of blood vessels [29]. Nevertheless, parathyroidectomy does not effectively treat hypertension in people with chronic kidney disease (CKD). On the other hand, the use of vitamin D as a treatment for secondary hyperparathyroidism results in a substantial decrease in blood pressure [30].

Dialysate Sodium Concentration

The salt concentration in the dialysate typically exceeds the level in the patient's serum, which can impact post-dialysis thirst, weight gain between dialysis sessions, and blood pressure levels. Furthermore, the administration of saline solution is frequently employed to achieve a favorable mineral equilibrium and uphold plasma volume while doing ultrafiltration to address instances of low blood pressure during dialysis. Modifying the programmed sodium levels from 155 meq/L to 135 mEq/L led to a decrease in the utilization of antihypertensive medications while maintaining the same predialysis blood pressure as when using a dialysate sodium concentration of 140 mEq/L [21-33].

4.2 Management of Hypertension in Dialysis Patients

Non-pharmacological Intervention

The management of hypertension in dialysis patients should focus on addressing the main cause of the condition, which is an excess of sodium and fluid in the body. This can be achieved by carefully adjusting the patient's weight to a desired level and avoiding the delivery of sodium during dialysis. Particular emphasis should be given to the fact that when dialysis is begun, 95% of patients already suffer from hypertension, and the majority are already prescribed

antihypertensive drugs. It is important to consider that the antihypertensive agent is commonly prescribed for other conditions, such as beta-blockers for angina symptoms, heart failure, or rate control, and renin-angiotensin inhibitors for heart failure. This information should be used as a guideline when deciding on the use of antihypertensive drugs if dry weight is still not achieved [4,34].

Achieving dry weight - Fluid volume expansion can be tracked through changes in body weight, and the rate of weight growth between dialysis sessions should not surpass 0.8 kg per day. Attaining desirable body weight in individuals undergoing dialysis is a multifaceted issue that necessitates the use of therapeutic expertise. Sinha and Agarwal defined dry weight as the minimum acceptable body weight after dialysis, attained by gradually reducing the weight until the patient has little to no symptoms of either low or high blood volume. Currently, there are no dependable clinical indicators available for accurately identifying the optimal dry weight. The degrees of leg edema often observed in dialysis patients are found to not correlate with objective measures that represent intravascular volume, such as measurements of inferior vena cava diameter, blood pressure monitoring, or plasma volume biomarkers. Bioimpedance techniques and blood pressure monitoring are increasingly employed to evaluate the fluid status of dialysis patients [4,35-6].

The patient's inability to maintain an ideal dry weight is a significant factor contributing to elevated blood pressure. An effective approach to accomplish this is by restricting the use of sodium. According to the previous study, restricting salt intake to 2 grams is predicted to result in an interdialytic weight increase of 1.25 kg over 2 days. Additionally, blood pressure is expected to decrease by around 4.2/2.0 mmHg to 5.2/3.7 mmHg. A weight gain of 2.5 kg or higher is linked to a notable rise in blood pressure. According to a study conducted by Aggarwal R, a reduction in dry weight of 1 kg resulted in a decrease in systolic blood pressure of approximately 6.6 mmHg and diastolic blood pressure of roughly 3.3 mmHg. Short daily dialysis and nocturnal hemodialysis aid in maintaining ideal body weight and blood pressure, although dialysis patients frequently experience nocturnal blood pressure surges [4,34-7].

Salt Limitation - Volume expansion resulting from excessive salt and water intake is a primary factor leading to hypertension in dialysis patients. However, it is only one component of the intricate pathophysiology that leads to hypertension in this particular group. Increased consumption of dietary salt is directly linked to higher mortality rates in people with HD. Decreasing salt consumption leads to decreased blood pressure in the overall population, individuals with high blood pressure from all ethnic backgrounds, individuals with and without diabetes, and patients with chronic kidney disease (CKD) [38-42].

A sudden shift in the concentration of sodium in the dialysate causes a corresponding change in the concentration of sodium in the blood plasma. A concise and meticulously conducted

intervention study revealed that decreasing the concentration of sodium in the dialysate resulted in a decline in plasma sodium levels and a simultaneous quick decrease in blood pressure among patients undergoing hemodialysis. This suggests a direct correlation between plasma sodium levels and blood pressure. Additional observational studies have established a connection between the salt levels in the blood before dialysis and the systolic blood pressure (SBP) and diastolic blood pressure (DBP) before dialysis. Modifications that affect plasma sodium levels are a subject of debate. It has been observed that lower plasma sodium levels are linked to higher mortality rates in dialysis populations. Additionally, in the general population, there appears to be a "U"-shaped relationship between plasma sodium levels and mortality, with the lowest mortality rates occurring within the range of 141 to 143 mmol/L. Multiple studies have been conducted to observe the effects of different levels of dialysate sodium (lower, neutral, and high) on maintenance hemodialysis patients. These studies employed various designs, including observational, parallel, and cross-over designs [43-7].

Regulating fluid volume and salt intake in dialysis patients is beneficial for limiting the activation of many cellular pathways, such as VEGF and nitric oxide, which can raise blood pressure. It also helps to reduce the activity of the renin-angiotensin-aldosterone system.

Dialysis Frequency - In a systematic review conducted by Shafiee et al, the effects of frequency and duration of hemodialysis on blood pressure optimization were examined. The study indicated that extended hemodialysis (EHD) can effectively decrease and stabilize blood pressure, leading to improvements in morbidity and mortality rates. [48]

When the duration of hemodialysis is short, the rapid removal of solutes from the patient's blood vessels leads to a sudden reduction in the osmolality of the fluid outside the cells. This results in the movement of fluid into the spaces between cells and inside cells, potentially resulting in swelling of the brain known as brain edema. Increasing the HD frequency will diminish the buildup of solutes and toxins. By combining this with an extended duration of hemodialysis, the intra-dialytic solute shift will be minimized and there will be a greater opportunity for equilibration. A minor change also results in reduced discomfort, less nausea, and an enhanced appetite for the patient. This facilitates a more equitable diet and obviates the need for the patient to consume excessive amounts of water to restore the reduction in plasma volume. [48]

Patients on standard hemodialysis typically consume approximately 1-2 liters of water daily. Following a standard hemodialysis schedule of three times per week, patients should expect to have an inter-dialytic weight increase of approximately 3-6 kg. The surplus volume must be eliminated within just 4 hours. A shorter interval between dialysis sessions in EHD results in a reduction in the volume of inter-dialytic fluid buildup. The process of fluid elimination during hemodialysis results in a reduced and less severe movement of fluid between the intracellular, interstitial, and extracellular compartments. Abundant amounts of salt and water have a

significant impact on increasing the blood pressure of patients with HD. Given that cardiovascular difficulties are the primary factors leading to death and illness in patients with HD, it can be said that salt and water are the most significant "uremic toxins." The retention of these substances is a serious worry and greatly affects the lives of patients. Reduced variability in the increase and decrease of volume leads to a decreased activation of the renin-angiotensin-aldosterone system (RAAS) and the release of catecholamines in EHD. This reduces the force applied parallel to the arterial walls and encourages more flexible blood vessels, leading to fewer harmful alterations in the arteries and a lower likelihood of developing vascular disease. [48]

Table 2 Nonpharmacological management to reduce sodium and fluid overload in dialysis patients

Achievement of individual dry weight
Minimization of inter- and intra-dialytic sodium increases
Limit sodium intake to less than 65 mmol (1.5-2 grams) per day
Reducing dialysate sodium in predialysis sodium in certain individuals
Avoid medications that contain sodium or sodium exchangers.
Avoid short dialysis durations (<4 hours)

Management of sleep apnea - Sleep apnea-induced hypoxemia can contribute to the development of hypertension. Obstructive sleep apnea (OSA) is commonly found in the general population and is often the underlying cause of secondary hypertension and resistant hypertension. According to reports, individuals with end-stage renal illness and severe obstructive sleep apnea (OSA) are seven times more likely to have resistant hypertension compared to the general population with high blood pressure. Fluid overload is seen as a contributing mechanism to the development of OSA in individuals undergoing dialysis. An investigation will be conducted to see if therapies for obstructive sleep apnea (OSA) can enhance blood pressure regulation and reduce mortality rates [49].

Pharmacological Treatment

When administering antihypertensive medications to individuals with stage 5 chronic kidney disease (CKD) who are undergoing dialysis, it is important to consider that the drugs' pharmacokinetics may be affected by the decreased ability of the kidneys to eliminate the drug and the process of dialysis. Furthermore, the efficacy of therapy may be influenced by factors such as adherence rates, adverse reactions, and financial burden. Additional issues that may occur in this specific group include low blood pressure during dialysis and blood clotting in the vascular access. Furthermore, several antihypertensive medications possess cardioprotective properties, hence diminishing the likelihood of mortality resulting from cardiovascular ailments. Some examples of these medications include renin-angiotensin-aldosterone system inhibitors, beta-blockers, calcium channel blockers (CCB), and aldosterone inhibitors (for patients who are not

undergoing dialysis). Angiotensin II is associated with endothelial dysfunction, smooth muscle proliferation, atherosclerotic plaque rupture, and left ventricular hypertrophy (LVH). Overall, the utilization of RAAS (renin-angiotensin-aldosterone system) decreases cardiovascular occurrences in individuals with vascular impairment and cases of stable coronary disease. Similarly, in individuals without chronic kidney disease (CKD), the use of beta-blocker treatment also leads to blood vessel protection [50-1].

ACE inhibitors (ACE-I) and angiotensin II receptor blockers (ARB) are pharmaceuticals approved by the JNC-8 and AHA/ACC guidelines as a recommended treatment for hypertension in people with chronic kidney disease (CKD). ACE inhibitors function by impeding the conversion of angiotensin I to angiotensin II, a powerful vasoconstrictor peptide. On the other hand, ARBs act by competitively blocking the angiotensin II receptors. The blockade leads to a decrease in the secretion of aldosterone, resulting in a reduction in peripheral vascular resistance and a consequent decrease in systemic blood pressure. The inhibition of angiotensin II also leads to the widening of the glomerular efferent arteriole, resulting in a decrease in intraglomerular pressure. This is believed to be the mechanism responsible for the protective impact of this medication on the kidneys. ACE inhibitors (ACE-I) and angiotensin receptor blockers (ARB) are prescribed to address proteinuria in chronic kidney disease (CKD). The renin-angiotensin-aldosterone system plays a direct role in the elimination of potassium in the distal nephron. Therefore, blocking this system can lead to hyperkalemia, which is an expected adverse effect of ACE-I and ARB. Consequently, it is not advisable to concurrently provide ACE-I and ARB due to the heightened occurrence of adverse effects [1,4,52].

Beta-blocker medications effectively manage hypertension by exerting their inhibitory influence on β receptors in heart tissue. Atenolol is efficiently eliminated by dialysis in comparison to lipophilic drugs like propranolol. Regardless of its effectiveness, beta blockers can be removed through dialysis. Certain long-acting drugs, including atenolol and lisinopril, can be administered three times per week [1,4,52].

Further consideration is given to the efficacy and tolerability of CCBs, as well as their positive impact on cardiovascular outcomes among patients undergoing dialysis. In one study, patients randomly assigned to amlodipine had a lower composite of all-cause mortality and CV events compared to those randomly assigned to placebo (hazard ratio [HR] 0.53, 95% CI 0.31-0.93). A clinically significant but statistically insignificant reduction in all-cause mortality was observed with amlodipine (12 percent versus 17 percent with placebo). Drug interactions with nondihydropyridine CCBs (e.g., verapamil or diltiazem) are frequent, and concurrent dosing with a BB may induce bradycardia. As a result, it's best to avoid using such agents [53].

5 Conclusion

Individuals having dialysis often have high blood pressure, which can be hard to treat and is linked to a higher risk of cardiovascular disease. The difficult nature of treating this illness is due to its complicated biology. Controlling too much fluid and salt is the best way to get the best blood pressure control. Too many of these things can set off cellular processes that raise blood pressure. Using pharmacological mixtures, like giving antihypertensive drugs like ACE-I or ARB, Beta-blockers, or CCBs together, can also be helpful.

REFERENCES

- [1] P. A. Sarafidis et al., "Hypertension in dialysis patients," *Journal of Hypertension*, Apr. 2017;35(4):657–76, doi: 10.1097/hjh.0000000000001283.
- [2] S. G. E. Buchares, K. K. S. Wallach, T. P. de Moraes, and R. Pecoits-Filho, "Hypertension in patients on dialysis: diagnosis, mechanisms, and management," *Brazilian Journal of Nephrology*, Sep. 2019;41(3):400–11, doi: 10.1590/2175-8239-jbn-2018-0155.
- [3] I. S. Kim, S. Kim, T.-H. Yoo, and J.-K. Kim, "Diagnosis and treatment of hypertension in dialysis patients: a systematic review," *Clinical Hypertension*, Sep. 2023;29(1). doi: 10.1186/s40885-023-00240-x.
- [4] J. T. Daugirdas, et al., "KDOQI Clinical Practice Guideline for Hemodialysis Adequacy: 2015 Update," *American Journal of Kidney Diseases*, Nov. 2015;66(5):884–930, doi: 10.1053/j.ajkd.2015.07.015.
- [5] W. McCallum and M. J. Sarnak, "Blood pressure target for the dialysis patient," *Seminars in Dialysis*, Nov. 2018;32(1):35–40, doi: 10.1111/sdi.12754.
- [6] M. Cozzolino, M. Mangano, A. Stucchi, P. Ciceri, F. Conte, and A. Galassi, "Cardiovascular disease in dialysis patients," *Nephrology Dialysis Transplantation*, 01-Oct-2018. [Online]. Available: <https://doi.org/10.1093/ndt/gfy174>.
- [7] H. X. Jie Liu, "Relationship between Nocturnal Blood Pressure and Left Ventricular Hypertrophy in Hypertensive Patients," *Journal of Hypertension- Open Access*, 2013;03(03), doi: 10.4172/2167-1095.1000151.
- [8] X. Yang et al., "Nighttime mean arterial pressure is associated with left ventricular hypertrophy in white-coat hypertension," *The Journal of Clinical Hypertension*, Jul. 2022;24(8):1035–43, doi: 10.1111/jch.14530.
- [9] M. Tadic et al., "The Prognostic Effect of Circadian Blood Pressure Pattern on Long-Term Cardiovascular Outcome Is Independent of Left Ventricular Remodeling," *Journal of Clinical Medicine*, Dec. 2019;8(12):2126, doi: 10.3390/jcm8122126.
- [10] P. I. Georgianos, P. A. Sarafidis, and C. Zoccali, "Intradialysis Hypertension in End-Stage Renal Disease Patients," *Hypertension*, Sep. 2015;66(3):456–63, doi: 10.1161/hypertensionaha.115.05858.
- [11] J. E. Flythe et al., "Blood pressure and volume management in dialysis: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference," *Kidney International*, May 2020;97(5):861–876, doi: 10.1016/j.kint.2020.01.046.
- [12] H. Wiig, F. C. Luft, and J. M. Titze, "The interstitium conducts extrarenal storage of sodium and represents a third compartment essential for extracellular volume and blood pressure homeostasis," *Acta Physiologica*, Dec. 2017;222(3), doi: 10.1111/apha.13006.
- [13] B. Afsar and R. E. Afsar, "The role of glycosaminoglycans in blood pressure regulation," *Microcirculation*, Oct. 2023;30(8), doi: 10.1111/micc.12832.
- [14] S. Beaini et al., "VEGF-C attenuates renal damage in salt-sensitive hypertension," *Journal of Cellular Physiology*, Oct. 2018;234(6): 9616–30, doi: 10.1002/jcp.27648.
- [15] Y. Shi, Y. Hu, B. Cui, S. Zhuang, and N. Liu, "Vascular endothelial growth factor-mediated peritoneal neoangiogenesis in peritoneal dialysis," *Peritoneal Dialysis*

- International: Journal of the International Society for Peritoneal Dialysis, Apr. 2021;42(1):25–38, doi: 10.1177/08968608211004683.
- [16] Y. S. Kim, “Is VEGF a new therapeutic target for hypertension in chronic kidney disease?” *Kidney Research and Clinical Practice*, Jun. 2013;32(2):49–51, doi: 10.1016/j.krcp.2013.04.008.
- [17] M. L. S. Sequeira-Lopez and R. A. Gomez, “Renin Cells, the Kidney, and Hypertension,” *Circulation Research*, Apr. 2021;128(7):887–907, doi: 10.1161/circresaha.121.318064.
- [18] J.-K. Kim et al., “Effects of Lowering Dialysate Calcium Concentrations on Arterial Stiffness in Patients Undergoing Hemodialysis,” *The Korean Journal of Internal Medicine*, 2011;26(3):320, doi: 10.3904/kjim.2011.26.3.320.
- [19] N. Lioufas, C. M. Hawley, J. D. Cameron, and N. D. Toussaint, “Chronic Kidney Disease and Pulse Wave Velocity: A Narrative Review,” *International Journal of Hypertension*, Feb. 2019;1–11, doi: 10.1155/2019/9189362.
- [20] J. H. Jeong, I. T. Fonkoue, A. A. Quyyumi, D. DaCosta, and J. Park, “Nocturnal blood pressure is associated with sympathetic nerve activity in patients with chronic kidney disease,” *Physiological Reports*, Oct. 2020;8,(20), doi: 10.14814/phy2.14602.
- [21] F. Quarti-Trevano, G. Seravalle, R. Dell’Oro, G. Mancina, and G. Grassi, “Autonomic Cardiovascular Alterations in Chronic Kidney Disease: Effects of Dialysis, Kidney Transplantation, and Renal Denervation,” *Current Hypertension Reports*, Feb. 2021;23(2) doi: 10.1007/s11906-021-01129-6.
- [22] Z. Ali, I. Riyadi, Y. A. Akbar, and K. Yakub Rahadiyanto, “Association of plasma asymmetric dimethylarginine concentration changes with intradialytic hypotension and hypertension in chronic hemodialysis patients,” *Journal of Physics: Conference Series*, Jul. 2019;1246(1):012003, doi: 10.1088/1742-6596/1246/1/012003.
- [23] P. Li, I. M. Schmidt, V. Sabbisetti, M. C. Tio, A. R. Opatowsky, and S. S. Waikar, “Plasma Endothelin-1 and Risk of Death and Hospitalization in Patients Undergoing Maintenance Hemodialysis,” *Clinical Journal of the American Society of Nephrology*, May 2020;15(6):784–93, doi: 10.2215/cjn.11130919.
- [24] J.-R. Chang et al., “Erythropoietin attenuates vascular calcification by inhibiting endoplasmic reticulum stress in rats with chronic kidney disease,” *Peptides*, Jan. 2020;123:170181, doi: 10.1016/j.peptides.2019.170181.
- [25] M. C. Foy, J. Vaishnav, and C. J. Sperati, “Drug-Induced Hypertension,” *Endocrinology and Metabolism Clinics of North America*, 2019;48(4):859–73, doi: 10.1016/j.ecl.2019.08.013.
- [26] P. Sun et al., “Epidemiologic and Genetic Associations of Erythropoietin With Blood Pressure, Hypertension, and Coronary Artery Disease,” *Hypertension*, Nov. 2021;78(5):1555–66, doi: 10.1161/hypertensionaha.121.17597.
- [27] J. Jamwal, S. M. Qadri, F. Siraj, and S. Shah, “Prevalence of obstructive sleep apnea in patients with chronic kidney disease: a hospital-based study,” *Sleep and Breathing*, Dec. 2022;27(5):1703–08, doi: 10.1007/s11325-022-02764-2.
- [28] L. Hui and R. Benca, “The Bidirectional Relationship Between Obstructive Sleep Apnea and Chronic Kidney Disease,” *Journal of Stroke and Cerebrovascular Diseases*, Sep. 2021;30(9):105652, doi: 10.1016/j.jstrokecerebrovasdis.2021.105652.
- [29] M. Simeoni, A. F. Perna, and G. Fuiano, “Secondary Hyperparathyroidism and Hypertension: An Intriguing Couple,” *Journal of Clinical Medicine*, Feb. 2020;9(3):629, doi: 10.3390/jcm9030629.
- [30] A. N. Graff-Baker, L. T. Bridges, Q. Chen, M. B. Faries, and M. Said, “Parathyroidectomy for Patients With Primary Hyperparathyroidism and Associations With Hypertension,” *JAMA Surgery*, Jan. 2020;155(1):32, doi: 10.1001/jamasurg.2019.3950.
- [31] X. Geng, Y. Song, B. Hou, Y. Ma, and Y. Wang, “The efficacy and safety of low dialysate sodium levels for patients with maintenance hemodialysis: A systematic review and meta-analysis,” *International Journal of Surgery*, Jul. 2020;79:332–9, doi: 10.1016/j.ijsu.2020.05.027.
- [32] S. V. Nair, K. Balasubramanian, A. Ramasamy, H. Thamizhselvam, S. Gharia, and S. Periasamy, “Effect of low dialysate sodium in the management of intradialytic hypertension in maintenance hemodialysis patients: A single-center Indian

- experience,” *Hemodialysis International*, Mar. 2021;25(3):399–406, doi: 10.1111/hdi.12921.
- [33] M. Wilkie and S. Davies, “Can Lower Dialysate Sodium Concentrations Contribute to Blood Pressure Control in Peritoneal Dialysis?,” *Peritoneal Dialysis International: Journal of the International Society for Peritoneal Dialysis*, Jul. 2019;39(4):297–8, doi: 10.3747/pdi.2019.00069.
- [34] Yaoxian Liang, Liangying Gan, Yulan Shen, Weihua Li, Dongliang Zhang, Zhongxin Li, et al., “Clinical characteristics and management of hemodialysis patients with pre-dialysis hypertension: a multicenter observational study,” *Renal Failure*, Oct. 2022;44(1):1821–28, doi: 10.1080/0886022x.2022.2136527.
- [35] J. E. Flythe and N. Bansal, “The relationship of volume overload and its control to hypertension in hemodialysis patients,” *Seminars in Dialysis*, Sep. 2019;32(6): 500–6, doi: 10.1111/sdi.12838.
- [36] O. A. Dhaybi and G. L. Bakris, “Hypertension and Chronic Kidney Disease Including Dialysis,” *Hypertension*, 2024:393–404, doi: 10.1016/b978-0-323-88369-6.00035-9.
- [37] I. S. Kim, S. Kim, T.-H. Yoo, and J.-K. Kim, “Diagnosis and treatment of hypertension in dialysis patients: a systematic review,” *Clinical Hypertension*, Sep. 2023;29(1), doi: 10.1186/s40885-023-00240-x.
- [38] T. W. R. Doulton, P. A. Swift, A. Murtaza, and I. Dasgupta, “Uncertainties in BP management in dialysis patients,” *Seminars in Dialysis*, Apr. 2020;33(3):223–35, doi: 10.1111/sdi.12880.
- [39] Grillo, Salvi, Coruzzi, Salvi, and Parati, “Sodium Intake and Hypertension,” *Nutrients*, Aug. 2019;11(9):1970, doi: 10.3390/nu11091970.
- [40] T. Filippini, M. Malavolti, P. K. Whelton, A. Naska, N. Orsini, and M. Vinceti, “Blood Pressure Effects of Sodium Reduction,” *Circulation*, Apr. 2021;143(16):1542–67, doi: 10.1161/circulationaha.120.050371.
- [41] F. J. He, N. R. C. Campbell, M. Woodward, and G. A. MacGregor, “Salt reduction to prevent hypertension: the reasons for the controversy,” *European Heart Journal*, 2021;42(25):2501–05, Jun. doi: 10.1093/eurheartj/ehab274.
- [42] N. I. Cole, P. A. Swift, F. J. He, G. A. MacGregor, and R. J. Suckling, “The effect of dietary salt on blood pressure in individuals receiving chronic dialysis: a systematic review and meta-analysis of randomized controlled trials,” *Journal of Human Hypertension*, Nov. 2018;33(4):319–26, doi: 10.1038/s41371-018-0131-5.
- [43] M. Wilkie and S. Davies, “Can Lower Dialysate Sodium Concentrations Contribute to Blood Pressure Control in Peritoneal Dialysis?,” *Peritoneal Dialysis International: Journal of the International Society for Peritoneal Dialysis*, Jul. 2019;39:4:297–98, doi: 10.3747/pdi.2019.00069.
- [44] C. Kourtidou, P. I. Georgianos, V. Vaios, and V. Liakopoulos, “Prescribing the optimal dialysate sodium concentration for managing hypertension and volume overload in hemodialysis: one size does not fit all patients,” *Journal of Human Hypertension*, Oct. 2023, Published, doi: 10.1038/s41371-023-00870-6.
- [45] X. Geng, Y. Song, B. Hou, Y. Ma, and Y. Wang, “The efficacy and safety of low dialysate sodium levels for patients with maintenance hemodialysis: A systematic review and meta-analysis,” *International Journal of Surgery*, Jul. 2020;79:332–39, doi: 10.1016/j.ijsu.2020.05.027.
- [46] S. V. Nair, K. Balasubramanian, A. Ramasamy, H. Thamizhselvam, S. Gharia, and S. Periasamy, “Effect of low dialysate sodium in the management of intradialytic hypertension in maintenance hemodialysis patients: A single-center Indian experience,” *Hemodialysis International*, Mar. 2021;25(3):399–406, doi: 10.1111/hdi.12921.
- [47] R. Radhakrishnan et al., “Effects of individualized dialysate sodium prescription in hemodialysis – Results from a prospective interventional trial,” *Indian Journal of Nephrology*, Jan. 01, 2020. https://doi.org/10.4103/ijn.ijn_391_18
- [48] Shafiee, Mohammad Ali, et al. “The Impact of Hemodialysis Frequency and Duration on Blood Pressure Management and Quality of Life in End-Stage Renal Disease Patients.” *Healthcare (Basel)* Sep. 2017;5(3): 52. doi:10.3390/healthcare5030052

- [49] Y. Taniyama, "Management of hypertension for patients undergoing dialysis therapy," *Renal Replacement Therapy*, 08-Jun-2016. [Online]. Available: <https://doi.org/10.1186/s41100-016-0034-2>.
- [50] A. D. Sinha and R. Agarwal, "Clinical Pharmacology of Antihypertensive Therapy for the Treatment of Hypertension in CKD," *Clinical Journal of the American Society of Nephrology*, Nov. 2018;14(5):757–64, doi: 10.2215/cjn.04330418.
- [51] T. W. R. Doulton, P. A. Swift, A. Murtaza, and I. Dasgupta, "Uncertainties in BP management in dialysis patients," *Seminars in Dialysis*, Apr. 2020;33(3):223–35, doi: 10.1111/sdi.12880.
- [52] V. Vaios, P. I. Georgianos, V. Liakopoulos, and R. Agarwal, "Assessment and Management of Hypertension among Patients on Peritoneal Dialysis," *Clinical Journal of the American Society of Nephrology*, Oct. 2018;14(2):297–305, DOI: 10.2215/cjn.07480618.
- [53] R. Agarwal, S. J. Schwab, G. L. Bakris, E.N. Taylor, "Hypertension in dialysis patients", *UpToDate*, Apr. 2023