



Hypertension in Pediatric Dialysis Patients: Etiology, Evaluation, and Management

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Published online: 8 June 2018
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Abstract

Purpose of Review Review epidemiology, pathophysiology, and management of hypertension in the pediatric dialysis population. **Recent Findings** Interdialytic blood pressure measurement, especially with ambulatory blood pressure monitoring, is the gold standard to assess for hypertension. Tools to assess dry weight aid in achievement of euvolemia, the primary therapy for management of hypertension. Persistent hypertension should be treated with antihypertensive medications and potentially with native nephrectomies. **Summary** Cardiovascular disease continues to be the primary cause of morbidity and mortality in the dialysis population with hypertension as an important modifiable factor. Achievement on dry weight and limiting both aggressiveness of interdialytic weight gain and ultrafiltration rate underlie the best approach. Tools to assess volume status beyond clinical assessment have shown promise in achieving euvolemia. When hypertension persists despite achievement of euvolemia, antihypertensive medications may be required and in some cases native nephrectomies. Future studies in children are needed to determine the best antihypertensive class and ideal rate of ultrafiltration on hemodialysis towards achievement of normotension and reduction of cardiovascular risk.

Keywords Pediatric dialysis · Hypertension · Hemodialysis · Peritoneal dialysis · Cardiovascular disease

Introduction

In the USA, there were 9672 children ≤ 21 years of age who received treatment for end-stage renal disease (ESRD), with an additional 10,251 adult survivors of childhood onset ESRD at the end of 2015 [1]. Internationally, the prevalence of ESRD in children 19 and younger ranges between 18 and 100 per million of age-related healthy population [2]. Cardiovascular disease is the major cause of morbidity and primary cause of mortality in the ESRD population for both adults and children [1, 3]. The United States Renal Data System [1] registry data demonstrated a mortality rate of 27 per 1000 patient years between 2010 and 2014. The primary cause of death was cardiac arrest with mortality due to cardiovascular disease accounting for close to 30% of the deaths [1]. Internationally, mortality is ~ 30 times higher among adults with childhood onset of dialysis as compared to

the general population, with cardiovascular disease accounting for 20–40% of the mortality [4, 5, 6]. Cardiovascular death rate is 1000 times higher among children and 100 times higher in young adults with ESRD as compared to the general population [6]. The cause of cardiovascular disease in ESRD is not completely understood and is likely multifactorial, including chronic inflammation, atherosclerosis, malnutrition, hyperphosphatemia, and hypertension.

Hypertension is an important modifiable risk factor for cardiovascular disease among ESRD patients. Among adults, the prevalence of hypertension, as defined as systolic blood pressure (BP) > 150 mmHg and diastolic BP > 85 mmHg, remains as high as 86% [7]. The North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) registry data of 2264 peritoneal dialysis (PD) and 1183 hemodialysis (HD) patients aged ≤ 21 years demonstrated hypertension (defined as blood pressure $> 90\%$ for age, gender, and height) in 41% of PD and 51% HD patients [8•]. Hypertension was more common among patients with glomerular cause of ESRD, < 6 years of age, and Black race [8•]. Internationally, among 851 PD and 464 HD pediatric patients from 15 countries, uncontrolled hypertension (defined as $> 95\%$ for age, gender, and height) was seen in 56.4% in PD and 63.8% in HD patients. Younger age, shorter dialysis vintage, and glomerular cause of ESRD were

This article is part of the Topical Collection on *Pediatric Hypertension*

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contributing factors to hypertension [9]. Pediatric studies have also demonstrated associations of hypertension with intermediate markers of cardiac morbidity such as left ventricular hypertrophy [10–12], increased carotid artery intimal-medial thickness [13], and coronary artery calcifications [14].

Volume excess from sodium and water retention is considered the primary etiology of hypertension in the dialysis population. Other factors include inappropriate activation of the renin-aldosterone-angiotensin system (RAAS), overactivity of the sympathetic nervous system (SNS), endothelial cell dysfunction, arterial stiffness, and iatrogenic from medications. Here we review the pathophysiology and management of hypertension in the dialysis population.

Blood Pressure Measurement

Ambulatory blood pressure monitoring (ABPM) is the gold standard towards assessment of hypertension, nocturnal hypertension, masked hypertension, and white coat hypertension, as it is for the healthy population. Particularly in HD, pre- and post-HD blood pressures provide an inaccurate estimate of interdialytic blood pressure burden as assessed by 44-h ABPM [15]. Blood pressures surrounding the HD procedure do not correlate with end organ damage such as elevated left ventricular mass index [16–18]. Forty-four-hour ABPM has demonstrated increased accuracy in detecting hypertension as compared to a 24-h assessment. Blood pressure loads > 25% on 44-h ABPM was associated with higher left ventricular mass index in children on chronic hemodialysis as compared to assessment with 24-h ABPM [19]. Home blood pressures correlate more closely with ABPM, end organ damage, and cardiovascular mortality when compared to peri-dialytic measurements [16, 20, 21]. Among 47 children on peritoneal dialysis, systolic blood pressure loads on 24-h ABPM were associated with increased risk of elevated left ventricular mass index [22]. In another study, ABPM was more sensitive in diagnosing hypertension as compared to casual blood pressures among 25 pediatric peritoneal dialysis patients (56 vs. 32%, $p < 0.05$) [23].

Sodium and Water Retention

Inability to excrete sodium and water is the leading cause of hypertension in the dialysis population. Retention of sodium and water leads to increased extracellular volume and therefore increased cardiac output. Normotensive children on dialysis tend to have increased residual urine output as compared to hypertensive children [24]. Increased interdialytic weight gain has also correlated with increased blood pressure loads on ABPM [24]. The relationship between volume excess and hypertension is not exact, as a normotensive person can be hypervolemic and a hypertensive person can be normovolemic.

This was demonstrated in a retrospective study that assessed 463 pre-HD BP assessment in 23 children over a year, relative to their hydration status as assessed by bioimpedance [25]. In the study, hypervolemia was defined as > 7% volume excess. Of the assessments that demonstrated hypertension, only 31% demonstrated hypervolemia, and 33% of the assessments that demonstrated normotension, hypervolemia was seen in 33% [25]. When hypertension is due to hypervolemia, achievement of normotension is often delayed by weeks after the achievement of normovolemia [26]. This observation is described as the “lag phenomenon.”

Dry Weight

Dry weight is defined as the body weight at the end of dialysis at which the patient can remain normotensive without antihypertensive medication, despite fluid accumulation, until the next dialysis treatment [27]. Stated differently, dry weight is the lowest weight a patient can tolerate without having symptoms of hypotension [27]. Thus, dry weight is often achieved by trial and error, and dry weight is thought to be achieved when the patient develops signs of hypotension, such as drop in blood pressure, cramping, yawning, headache, or abdominal pain. Complicating this further is that a patient may display signs of intravascular volume depletion despite being in salt and volume excess due to the aggressiveness of the ultrafiltration, or impaired ability for physiologic vasoconstriction during ultrafiltration due to vasodilatory antihypertensive medications.

Clinical assessment of dry weight includes monitoring weight, presence of edema, jugular venous distension, and crackles on lung auscultation in patients with volume excess and symptoms of orthostasis, sunken eyes, and hypotension in those with intravascular volume depletion. The clinical assessment is inaccurate in states of more subtle volume excess of depletion. Markers such as weight are further confounded in a growing child. Due to the limitations of relying on clinical assessment of dry weight, different techniques have been studied to aid in assessment and achievement of dry weight (Table 1). Biochemical markers include atrial natriuretic peptide, cyclic guanidine monophosphate, brain natriuretic peptide, and troponin T [28, 29]. Most of the biomarkers can be affected by various factors other than volume status, thus limiting their clinical utility. Ultrasound measurement of inferior vena cava diameter and its collapsibility is a simple and non-invasive way to assess intravascular volume status. Challenges that prevent broad use include inter-operator error and patient variability in diameter measurements [27, 29].

Bioelectrical impedance analysis, or bioimpedance, is a method that determines the electrical opposition (impedance) to the flow of an electric current through the body. The analysis using alternating current to determine total body water can be determined as a single frequency or multi-frequency.

Table 1 Tools for volume assessment

Tool	Advantages	Disadvantages
Biochemical markers*	<ul style="list-style-type: none"> • Easy to obtain, especially on hemodialysis 	<ul style="list-style-type: none"> • Can be affected by factors other than volume status
Inferior vena cava diameter	<ul style="list-style-type: none"> • Non-invasive 	<ul style="list-style-type: none"> • Inter-operator error • Patient variability—no population normalization • Measures relative intravascular volume status only • Does not assess body volume status
Bioimpedance	<ul style="list-style-type: none"> • Non-invasive • Can assess body volume status and relative water distribution 	<ul style="list-style-type: none"> • Results affected by dialysis and patient factors
Lung ultrasound	<ul style="list-style-type: none"> • Non-invasive • Correlates well with volume excess 	<ul style="list-style-type: none"> • Need training on ultrasound
Relative plasma volume monitoring	<ul style="list-style-type: none"> • Non-invasive • Permits avoidance of hypotension from aggressive ultrafiltration 	<ul style="list-style-type: none"> • Measures relative intravascular volume only • Will be inaccurate during blood transfusion • Cannot be utilized on PD

*Atrial natriuretic peptide, cyclic guanidine monophosphate, brain natriuretic peptide, and troponin T

The addition of multi-frequency allows the ability to distinguish between intracellular and extracellular compartments [27, 29]. In adults, bioimpedance analysis has shown that extracellular volume change correlated with the ultrafiltration volume [30]. Using multi-frequency bioimpedance, HD patients demonstrated expanded extracellular space pre-dialysis as compared to healthy controls, and HD patients that demonstrated underhydration as compared to controls experienced more intradialytic hypotension [31]. Other studies in adults using bioimpedance have demonstrated underestimation of ultrafiltration volumes by 30% based on ECF volumes pre- and post-HD [27]. Pediatric studies have demonstrated the utility of this technique, showing good correlation of measured blood volume change to percentage body weight change [32], and serial clinical use to assess dry weight at a single center led to improvement in the medial left ventricular mass index and reduction in the left ventricular hypertrophy [33]. The technology does have limitations. Temperature and ion changes that occur during dialysis may affect electrical impedance, as may patient factors such as electrolyte imbalance, hematocrit values, and protein levels [27].

Lung ultrasound has been used to assess volume status. In the setting of extracellular fluid excess, hydrostatic forces will create a transudative effusion that leads to a decrease in the acoustic mismatch between lung and surrounding tissues. This creates a partial reflection and discrete hyper-echogenic reverberation of the ultrasound beam arising from the pleural line known as “B-lines” [34]. In adults, lung ultrasound findings including B-lines correlated with other markers of fluid overload including clinical parameters [35, 36], B-type natriuretic peptide, inferior vena cava diameter, and bioimpedance [37, 38]. B-lines are not present in euvoletic patients and appear before clinical signs of volume excess [35, 39, 40]. In a single-center study of 96 patients on HD in which lung ultrasound, bioimpedance, and

echocardiography were prospectively studied for their ability to predict mortality, pre-dialysis B-line score and left ventricular mass index were significantly associated with survival times [41]. A recent pediatric study that included patients with end-stage renal disease on both modalities of dialysis and patients with acute kidney injury demonstrated a significant correlation between B-lines and volume excess as determined by target weight [34]. Among 13 children on dialysis in which objective parameters of volume excess were studied including lung ultrasound, bioimpedance, clinical parameters, and inferior vena cava parameter, only lung ultrasound correlated significantly with volume overload [34, 42].

Relative plasma volume monitoring during HD provides insight into the relative rate of ultrafiltration compared to the rate of refilling of plasma volume from the extravascular space. Photo-optical technology measures hematocrit or protein values. Increase in hematocrit or protein concentration is inversely proportional to the change in plasma volume [27]. The graph is displayed as 1/hematocrit, where a downward slope reflects a decrease in plasma volume and therefore intravascular volume. A flat slope will reflect similar rates of ultrafiltration and refilling. A steep downward slope reflects an ultrafiltration rate that is faster than the refilling rate. This technology can also be used to prevent aggressive ultrafiltration and prevent intradialytic hypotension. The use of this technology in adults has led to mixed results with some reporting improvement in dry weight [43, 44] and some reporting improvement in casual blood pressures [45] and lower systolic blood pressure as measured by 44-h ABPM [46]. A randomized trial utilizing plasma volume monitoring was associated with higher access-related hospitalization and mortality [47]. Although the authors of the study and others have cautioned generalizations of the study due to atypically low hospitalization rates and mortality of the control group, and an observation that the control group may have received a more

aggressive reduction in post-dialysis weight [47, 48], several pediatric studies have studied the use of plasma volume monitoring [49, 50, 51, 52]. In a multicenter prospective study of 20 pediatric patients, plasma volume monitoring was used to target 100% ultrafiltration goal with 50% to be removed in the first hour (max plasma volume change of 8–12% per hour) and the remaining 50% over the subsequent time (max plasma volume change of 5% per hour) [51]. They demonstrated a decrease in dialysis associated morbidity, reduction in antihypertensive medication, and improved ABPM profiles. There was no change in weight or left ventricular mass index at the end of the 6-month study [51]. In 9 pediatric HD patients, the use of plasma volume monitoring to challenge dry weight and reduce antihypertensive use systematically over four phases (each phase more aggressively challenging dry weight) resulted in mean dry weight reduction, decreased blood pressure measured both casually and by ABPM, and a reduction in antihypertensive burden. There was a notation of increased intradialytic symptoms when weight was actively challenged in the later phases, but this did not reach statistical significance [52].

A recent study that compared various methods of assessment of volume status in chronic HD patients demonstrated that B-line scores with lung ultrasonography were more accurate in predicting overhydration as compared to bioelectrical impedance analysis and continuous volume monitoring when measured by inferior vena cava diameter [53]. A pragmatic and more accurate approach for assessment of volume status may be to utilize many if not all of the tools at the clinicians' disposal as described by Ronco et al. [54].

Dietary Sodium Intake

The link between sodium intake and hypertension has been known since at least 1700 BC [26] and has been confirmed by modern studies dating to the 1950s when cultures with low salt intake were noted to have low normal blood pressures, even in elderly age [26, 55, 56]. The observation that dietary sodium restriction and ultrafiltration led to improved blood pressure management was noted by Belding Scribner when treating the first patient to receive chronic dialysis, who suffered from malignant hypertension [57]. Controlling dietary sodium intake facilitates achievement of dry weight [58] and is associated with decreased thirst, lower interdialytic weight gain, improved blood pressure control, lower LVMI, and decreased mortality in adults [59–61]. Despite guidelines recommending limiting sodium intake in children with kidney disease and hypertension between 1500 and 2300 mg depending on the age [62], data from a registry of children with chronic kidney disease demonstrated that sodium intake in children with chronic kidney disease stages 2–4 was greater than 3000 mg daily with 25% of adolescents consuming more than 5000 mg of sodium per day [63]. A study looking at sodium intake among school-aged children found that the top ten

food categories that contributed to 48% of the salt intake are from processed foods, with the exception of milk, which naturally has sodium [64]. Similar results of US adults demonstrated that 70.9% of the salt consumed was sodium added to food outside the home [65]. Here, renal dieticians become key members of the treatment team by educating the patient and their family on low-sodium food with high nutritional content. The social worker can also play a role by providing better access to these often more expensive foods.

Optimization of Dialysis

Duration of therapy and concentration of dialysate sodium for hemodialysis have changed in the USA since chronic dialysis became possible in the 1960s. Clyde Shields', the first chronic dialysis patient, initial prescription consisted of hemodialysis therapy lasting up to 76 h every week with dialysate sodium of 130 mEq/L [66]. Over time, dialysis prescriptions evolved to 20-h sessions twice a week with the goal of controlling blood pressure and reducing the progression of peripheral neuropathy [67]. After the seminal National Cooperative Dialysis Study (NCDS) [68] determined that efficiency of urea clearance and not time was important for patient survival, short dialysis consisting of 3–4-h sessions three times a week was practiced in the 1980s [67]. The dialysate sodium concentration gradually increased from 134 to 136 in the 1980s to 136–149 from 2010 to 2015 [67]. Supra-physiologic sodium concentrations were used to reduce intradialytic hypotension that occurred as ultrafiltration rates needed to be increased to achieve the appropriate volume reduction in a shortened period. The practice of modifying sodium concentration in the dialysate over the course of the dialysis session, termed sodium modeling, did lead to better patient tolerability of hemodialysis due to reduced intradialytic hypotensive episodes [69], although the decreased clearance of sodium and at times increased sodium delivery to the patient resulted in increased interdialytic thirst, higher interdialytic weight gain, increased hypertension, and intradialytic hypotension [70, 71].

Currently, there is increasing evidence that reduction in dialysate sodium at or slightly below the patient's pre-dialysis serum concentration leads to reduction in thirst, interdialytic weight gain, and hypertension [66, 72, 73]. A small pediatric study consisting of 5 patients demonstrated a reduction in interdialytic weight gain and pre-dialysis blood pressure when dialysate sodium was reduced from 140 to 138 mEq/L [73]. A systematic review of 23 studies comparing high vs. low dialysate sodium concentration in chronic adult hemodialysis patients demonstrated that blood pressure was unaffected by the concentration of dialysate sodium. There was an increase in interdialytic weight gain in the higher dialysate sodium group and increased intradialytic hypotension in the low dialysate sodium group [74]. Mortality was assessed in three observational studies and

overall demonstrated reduced mortality with higher dialysate sodium concentrations, but was confounded by patients' serum sodium concentrations, which demonstrated an inverse relationship between serum sodium concentration and death [74–76]. Specifically, an international study by Hecking et al. demonstrated lower serum sodium (< 137 mEq/L) was associated with the highest risk of death, and in that group dialyzing against a bath > 140 mEq/L was protective [75].

Increasing dialysis treatment time is another factor associated with improved outcomes. The recommendations from the European Best Practice Guidelines include a minimum duration of dialysis of 4 h three times a week [77]. As per the Clinical Performance Project Measures Project analysis of 32,065 patients from 2004 to 2007, only 25% received dialysis greater than 4 h per session while 25% received < 3 h and 15 min of dialysis [78]. Adult and pediatric studies have demonstrated improved control of blood pressure, faster achievement of dry weight, and reduction in medication burden including antihypertensive medications with increased dialysis time [79, 80, 81, 82–88]. Increasing time also allows to reduce ultrafiltration rate which reduces the risk of myocardial stunning [89]. Current recommendation in adults is to reduce ultrafiltration rate to < 13 ml/kg/h, but even rates > 10 ml/kg/h are associated with increased morbidity and mortality [90, 91, 92]. Myocardial stunning is not limited to adults as a pediatric study consisting of 12 patients of whom 11 demonstrated myocardial stunning which was associated with intradialytic blood pressure reduction. In this study, there was no association with ultrafiltration rate and stunning [93].

Optimization of sodium and water removal in peritoneal dialysis can be achieved by managing osmotic potential (adjusting dextrose concentration and dwell time) and surface area recruitment and hydrostatic pressure (adjusting fill volume). The three-pore model theory of peritoneal transport describes three various-sized pores of the peritoneal endothelium through which transports of water and solutes are transported. The smallest are aquaporin channels via which only water can be transported that are activated by hyperosmolar state created by dextrose-based solutions, small pores that allow small solutes and water, and large pores that transport macromolecules [94]. Water removal is optimized by short dwell times to maintain the higher osmotic potential by a higher dextrose concentration, and lower fill volumes to reduce hydrostatic pressure that would counteract the osmotic potential [95]. In contrast, solute removal, including sodium, is optimized by increased fill volumes to optimize recruitment of the surface area and longer dwell time [95]. Using a higher dextrose concentration also leads to more glucose degradation products that are toxic to the peritoneum [96]. Another polymer of maltodextrin that is produced by the metabolism of cornstarch offers an alternative to dextrose, named icodextrin. Icodextrin is absorbed from the peritoneal space much more slowly via the lymphatics and thus maintains the osmotic potential longer. It further exerts its effect via colloid osmosis and therefore has its effects via the small pores and not the aquaporin

channels, thus leading to less sodium sieving [97]. A recent retrospective study of 50 pediatric patients who had icodextrin as their fluid for the long day dwell demonstrated improved ultrafiltration and reduced absorption of icodextrin at fill volumes above 550 ml/m², and improved ultrafiltration with increasing age, with the youngest patients absorbing more icodextrin [98]. Icodextrin is only meant to be used for the long dwell, as metabolism over time increases its colloid potential. Studies in adults have demonstrated equivalent ultrafiltration of icodextrin over 10 h and superior beyond that time as compared to 4.25% dextrose solutions [99, 100]. Adapted automated peritoneal dialysis is where the peritoneal dialysis machine will alternate between short dwells with low fill volumes to enhance ultrafiltration and long dwells with large fill volumes to enhance solute clearance [101, 102]. In a prospective, crossover study in adults, adaptive peritoneal dialysis resulted in increased sodium and water removal and improved blood pressures as compared to conventional peritoneal dialysis [102].

Diuretics

Diuretics have no benefit in anuric patients, even at high doses given intravenously [103]. In patients with preserved residual renal function, loop diuretics may enhance urine output and limit interdialytic weight gain [104]. There are no data for cardiovascular benefit or safety of diuretics in dialysis patients, and specific studies in pediatric patients are lacking.

Volume-Independent Causes of Hypertension

The renin-angiotensin-aldosterone system (RAAS) is a well-established cause of hypertension in chronic kidney disease and in ESRD [105]. Among 51 HD patients, plasma renin activity (PRA) was higher among patients who had uncontrolled hypertension as compared to those whose blood pressure was controlled by ultrafiltration and sodium restriction [105]. Among the 18 who had uncontrolled hypertension, 17 had significant improvement in blood pressure after native nephrectomies [105]. Angiotensin II and aldosterone both contribute to left ventricular hypertrophy and endothelial cell dysfunction that is independent of blood pressures [106]. A pediatric study compared RAAS between 32 healthy normotensive controls, 23 normotensive children with chronic kidney disease, 34 hypertensive children with chronic kidney disease, and 21 children with ESRD. PRA and angiotensin I, II, and (1–7) were higher in hypertensive patients with chronic kidney disease as compared to normotensive children with chronic kidney disease and healthy controls [107]. Treating patients with chronic kidney disease with angiotensin-converting enzyme inhibitors (ACEi) resulted in increased angiotensin 1–7 and decreased angiotensin II, whereas ESRD patients with ACEi therapy did

not have a decrease in angiotensin II levels [107]. This may explain why refractory hypertensive ESRD patients may benefit from native nephrectomies.

ESRD patients are also known to have increased sympathetic nervous system activity [108]. The etiology of the increased sympathetic nervous system activity may be from the diseased native kidney. This was determined in an elegant study in transplant recipients who had continued elevation of the sympathetic nervous system until they had native nephrectomies [109]. In pediatrics, there has been a documentation of increase in catecholamines on HD during episodes of intradialytic hypotension [110]. Elevated sympathetic nervous system activation has been implicated in blunted nocturnal dipping [111] and increasing frequency of dialysis from three times a week for 4 h to six times a week for 2 h seems to result in lowering sympathetic nervous system activity [106, 112].

Arterial stiffness which occurs as a consequence of arteriosclerosis is seen naturally with aging but is accelerated in chronic disease states such as diabetes and chronic kidney disease/ESRD. Increased arterial stiffness is associated with increased risk of cardiovascular disease and mortality in adults [113]. Evidence exists of premature arterial stiffness in pediatric ESRD patients with correlations to a diagnosis of hypertension [106, 114].

Other factors implicated as an underlying cause of non-volume-dependent hypertension in ESRD patients include medications such as erythropoietin stimulating agents [115], endothelial cell dysfunction that results from an imbalance of endothelial cell-derived nitric oxide and endothelin-1 resulting in vasoconstriction [106, 116], inability to degrade catecholamines due to a lack of renalase which is usually secreted by the kidney [117], and other factors also leading to atherosclerosis such as oxidative stress and inflammation [106].

Antihypertensive Medications

With the exception of diuretics, all classes of antihypertensive medications are useful in blood pressure control in the dialysis population. Antihypertensive medications are ineffective when volume excess is the etiology of hypertension and studies have demonstrated hypertension to be associated with increased antihypertensive use [118]. Among uncontrolled hypertensive patients on antihypertensive medication in the Chronic Kidney Disease in children (CKiD) Study, uncontrolled hypertension was associated with absence of ACEi or angiotensin receptor blockers (ARB) [119]. A prospective study in the same cohort also demonstrated that antihypertensive use other than ACEi or ARB predicted increased left ventricular mass index [120]. A recent adult randomized control trial, among hypertensive chronic hemodialysis patients with left ventricular hypertrophy, compared the effectiveness of Lisinopril vs. Atenolol given three times a week post-dialysis towards regression of the left ventricular

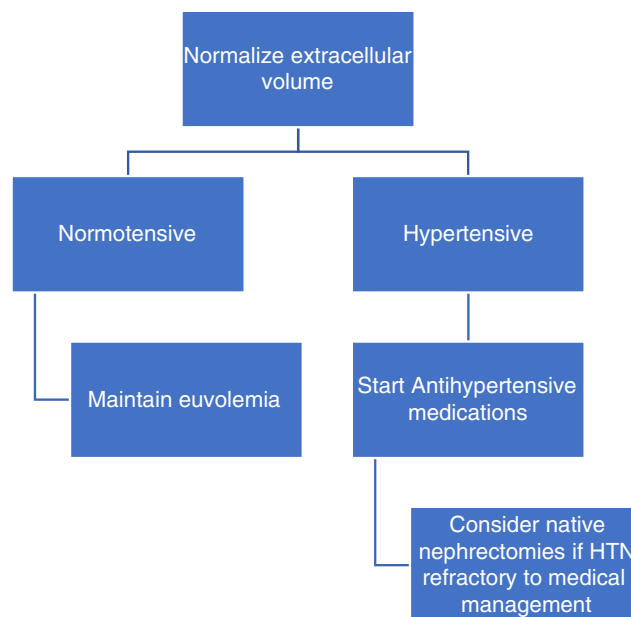


Fig. 1 Approach to management of hypertension in pediatric dialysis patients

hypertrophy [121]. Both medications produced similar results in blood pressure improvement based on 44-h ABPM and in regression of left ventricular hypertrophy. When monthly home blood pressures were assessed, the Lisinopril group had higher blood pressures despite a greater number of antihypertensive agents and reduction in dry weight. The study was also stopped early due to increased risk of cardiovascular morbidity and mortality in the Lisinopril group as compared to the Atenolol group [121].

Pharmacokinetics and volume of distribution of the choice of antihypertensive should be considered. Water-soluble medication will be cleared during dialysis. This may be beneficial if patients suffer from intradialytic hypotension, but may be a contributing factor in those suffering from intradialytic hypertension. When medication noncompliance is a barrier, post-dialysis medication administration as described in the study above may be beneficial.

Conclusion

Hypertension is an important modifiable factor among patients on dialysis, whose primary cause of morbidity and mortality is cardiovascular disease. Achievement on dry weight and limiting both aggressiveness of interdialytic weight gain and ultrafiltration rate underlie the best approach. Utilization of tools to assess volume status beyond clinical assessment has shown promise in achieving normotension. When hypertension persists despite achievement of euolemia, antihypertensive medications may be required and in some cases native nephrectomies (Fig. 1).

Compliance with Ethical Standards

Conflict of Interest The authors declare no conflicts of interest relevant to this manuscript.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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