Pediatr Nephrol (2018) 33:239–250
DOI 10.1007/s00467-017-3666-8

EDUCATIONAL REVIEW

Blood pressure management in children on dialysis

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Received: 17 December 2016 / Revised: 27 March 2017 / Accepted: 27 March 2017 / Published online: 9 June 2017

Abstract Hypertension is a leading cause of cardiovascular complications in children on dialysis. Volume overload and activation of the renin–angiotensin–aldosterone system play a major role in the pathophysiology of hypertension. The first step in managing blood pressure (BP) is the careful assessment of ambulatory BP monitoring. Volume control is essential and should start with the accurate identification of dry weight, based on a comprehensive assessment, including bioimpedance analysis and intradialytic blood volume monitoring (BVM). Reduction of interdialytic weight gain (IDWG) is critical, as higher IDWG is associated with a worse left ventricular mass index and poorer BP control: it can be obtained by means of salt restriction, reduced fluid intake, and optimized sodium removal in dialysis. Optimization of peritoneal dialysis and intensified hemodialysis or hemodiafiltration have been shown to improve both fluid and sodium management, leading to better BP levels. Studies comparing different antihypertensive agents in children are lacking. The pharmacokinetic properties of each drug should be considered. At present, BP control remains suboptimal in many patients and efforts are needed to improve the long-term outcomes of children on dialysis.

Keywords Blood pressure · Dialysis · End-stage renal disease · Blood volume monitoring · Sodium overload · Volume overload · Children

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Introduction

Despite significant advances in the management of children with end-stage renal disease (ESRD), life expectancy in this population remains significantly lower than in healthy children [1–3]. Recent data have shown a 5-year survival probability of 89% for children with ESRD, with a lower survival rate in those undergoing hemodialysis (HD) and peritoneal dialysis (PD; 76% and 81% respectively) compared with transplant recipients (95%) [2, 3]. Similarly, the mortality rate of young adults with childhood-onset ESRD is higher than that of the general population. The average life expectancy of patients with a functioning graft at 18 years of age is 63.2 years, whereas for those remaining on dialysis it drops to 38.2 years [1]. Cardiovascular disease is the leading cause of death [1–3]. Several traditional and nontraditional cardiovascular risk factors have been identified. Although uremic risk factors, such as abnormal mineral metabolism, are associated with the early development of arteriosclerosis, arterial hypertension (HTN) remains the most common modifiable risk factor for the occurrence of cardiomyopathy in this population [4, 5]. Given that most cardiovascular deaths in children on dialysis are due to cardiac arrest, arrhythmia or congestive heart failure, cardiomyopathy is generally considered the main pathogenic mechanism of early cardiovascular events [1–3]. The appropriate management of blood pressure (BP) is therefore mandatory for the prevention of short- and long-term consequences. This review summarizes current knowledge concerning the management of BP in children on dialysis.

Prevalence of HTN in children on dialysis

Epidemiological data on BP control in dialyzed children mainly derive from large registry-based studies considering casual BP levels (Table 1) [6–8]. In these studies, HTN was

Table 1 Prevalence of hypertension (*HTN*) in children on hemodialysis (*HD*) and peritoneal dialysis (*PD*; %)

Dialysis modality	Reference	Number of patients	HTN	Controlled HTN	Untreated HTN	Uncontrolled HTN	Patients taking antiHTN drugs	Uncontrolled HTN in treated patients
HD	Kramer et al. [7]	464	69.7	24.2	45.5		58.2	63.8
	Halbach et al.[a] [8]	1,183	84	13	20	51	63.1	80
	Chavers et al. [6]	624	79.2	16.3	16.8	46.1	62	74
PD	Kramer et al. [7]	851	68.2	32.7	35.5		52	54.6
	Halbach et al.[a] [8]	2,264	81	14	26	13.4	55	74.5
	Bakkaloglu et al. [5]	507	69.8	30	41	26.4	56.4	46.8

HTN either systolic or diastolic blood pressure z score > 95th percentile or receiving antihypertensive medications, *controlled HTN* both systolic and diastolic blood pressure z score < 95th percentile and receiving antihypertensive medications, *untreated HTN* either systolic or diastolic blood pressure z score > 95th percentile and not receiving antihypertensive medications, *uncontrolled HTN* either systolic or diastolic blood pressure z score > 95th percentile and receiving antihypertensive medications

[a] 90th percentile used instead of 95th percentile

commonly defined as systolic or diastolic BP above the 95th percentile for age, height, and sex, or according to the use of antihypertensive medications. In keeping with this definition, 70–84% of children on HD and 68–81% of those on PD were classified as hypertensive [6–8]. Moreover, BP was poorly controlled in 55–80% of patients receiving antihypertensive medications [6–8].

A few single-center studies have investigated the BP profile of children receiving maintenance dialysis by means of ambulatory blood pressure monitoring (ABPM). Chaudhuri et al. assessed HTN prevalence by means of 24-h ABPM in 24 children on dialysis and found that 42% and 46% of them had significantly elevated daytime systolic and diastolic loads respectively, 58% had an elevated night-time systolic load, and 71% had an elevated night-time diastolic load [9]. Fluid overload and hypertension also represent a frequent cause of morbidity, accounting for 41% of hospitalizations in children on hemodialysis at the Texas Children's Hospital [10].

As regards the risk factors for poor BP control, HTN was associated with younger age, shorter duration of renal replacement therapy, glomerular diseases, and, in some reports, HD as dialysis modality [6–9].

Etiopathogenesis of HTN in children on dialysis

Arterial HTN in children on dialysis is a complex and multifactorial problem. Sodium (Na) retention and volume overload have traditionally been considered the main causes of HTN in adult patients with ESRD: strict volume control and salt restriction decreased mean BP values from 150/89 to 121/75 in 218 HD patients, with only 9 requiring a drug (enalapril) to reach this goal during a follow-up of 47 ± 34 months [11]. Some pediatric studies have confirmed this relationship. In a study involving 71 children on HD, hypertensive subjects had significantly higher average post-HD excess weight above dry-weight than patients with normal BP [12]. Interdialytic weight gain (IDWG) correlated significantly with systolic and diastolic BP in a recent study involving 16 oligo-anuric children receiving chronic HD [13]. In the same way, higher IDWG was significantly associated with higher BP load on 44-h ABPM in 13 pediatric patients on HD [14]. In a Polish multicenter study, both systolic and diastolic BP correlated positively with residual urine output and daily ultrafiltration in children on PD, thus confirming the importance of adequate fluid balance in this population [15].

Activation of the renin–angiotensin–aldosterone system (RAAS), sympathetic nervous system activity, endothelial dysfunction, hyperparathyroidism, and drugs, such as erythropoietin, glucocorticoids, and calcineurin inhibitors, have all been described as possible causes of HTN in children with ESRD [16, 17]. An in-depth review of the pathogenic aspects of HTN in children with CKD is beyond the aims of the present paper and has been described in detail elsewhere [16, 17].

BP assessment

Blood pressure values are strongly influenced by settings and assessment modality. Three methods of BP assessment in children are available: casual office BP, home BP, and ABPM.

Casual pre- or post-HD office BP is the most commonly described method in the pediatric literature [6–8] and is prevalent in clinical practice, but it has several limitations. It only gives a snapshot of a continuously changing phenomenon and it is strongly influenced by measurement conditions. Home BP allows for more reliable BP assessment and significantly reduces the effects of venipuncture, white coat phenomenon, pre-HD fluid overload, and dialysis ultrafiltration. Adult

studies have demonstrated a better correlation between home BP and ABPM rather than pre- or post-HD BP and a better predictive value for target organ damage [18]. BP has been reported to rise in adults on HD at a rate of 4 mmHg every 10 h after dialysis [19], which means that the pre- and post-HD readings are of little value in interpreting the overall BP control of a patient. A true validation of the accuracy of home BP monitoring has never been performed in children with ESRD, and a clear association with target organ damage in this population is lacking.

Compared with casual BP measurements, 24-h ABPM has several advantages, as it allows for the identification of children with white-coat HTN, nocturnal HTN, and masked HTN (normal office BP, but abnormal ABPM), which has been associated with left ventricular hypertrophy (LVH) in children with CKD [20]. It also provides data on BP and heart rate variability; children with CKD and uncontrolled BP have a higher BP variability and lower heart rate variability compared with normotensive CKD subjects, which are considered markers of sympathetic nervous system hyperactivity and autonomic nervous system dysfunction respectively [21]. Chaudhuri et al. demonstrated that the prevalence of HTN in children on dialysis was significantly higher when diagnosed by ABPM compared with office BP [9]. The same authors showed that children with LVH had higher daytime and night-time systolic and diastolic BP loads and a lesser degree of nocturnal dipping of systolic BP, compared with those without LVH [9]. Data from the American Chronic Kidney Disease (CKiD) cohort showed that the risk of masked HTN was very low in children with casual BP <25th percentile, suggesting that ABPM could probably be omitted in CKD children with BP in the low–normal range [22]. ABPM is usually considered a reliable method of BP assessment in children older than 5 years only: although some studies reporting on its use in younger children have been published, normative data exist for children older than 5 years only and most of the studies in children on dialysis excluded small children [23]. Forty-four-hour ABPM has been proposed in patients on chronic thrice-weekly HD to overcome the impact of interdialytic fluid variability [14]. In a recent study on 13 children on chronic HD, a higher percentage of patients were diagnosed with HTN following 44 h as opposed to 24-h ABPM; children with 44-h BP loads ≥25% on 44-h ABPM had significantly higher LVMI than those with normal BP, whereas this association was not found with 24-h ABPM [14].

To summarize, ABPM should be considered the gold standard for BP assessment in children on dialysis. Pre- and post-HD casual BP measurements are very poor markers of BP control, whereas home BP evaluation is more reliable. ABPM is mandatory in the case of inconsistency between markers of target organ damage and office/home BP measurements, that is, in children with abnormal echocardiographic findings and normal office/home BP, or normal LVMI with high casual BP (Fig. 1). It could probably be omitted in those with casual BP <25th percentile and normal echocardiography, and delayed after treatment in hypertensive children with impaired LVMI. It seems advisable that patients with BP between the 25th and 90th percentile without signs of target organ damage undergo ABPM at least annually. Monitoring should start at the end of a mid-week HD session or during daytime hours for PD patients. ABPM should not be used in children younger than 5 years of age because of its low reliability in this age group.

Consequences of HTN

Large studies investigating the association between BP and hard outcomes such as mortality or cardiovascular events have to our knowledge never been performed in children on dialysis. Unequivocal data have demonstrated an association between HTN and intermediate cardiovascular outcomes, such as LVH and increased carotid intima-media thickness (cIMT) [5, 9, 14, 24, 25].

Based on a cross-sectional analysis of 507 children on PD, the International Pediatric Peritoneal Dialysis Network (IPPN) Registry reported an overall LVH prevalence of 48.1% [5]. The most important determinant of LVH was BP: the risk of developing LVH was more than double in patients with systolic HTN. The systolic office BP was 7 mmHg higher in children with persistent or de novo LVH than in children with normal LV mass [5]. In a single-center study involving 17 children on HD, Ulinski showed a prevalence of LVH of 82% at the beginning of dialysis, which decreased to 41% after a median follow-up of 16 months: LVMI correlated significantly with systolic, diastolic, and mean BP levels [24]. This correlation was confirmed by 24-h and 44-h ABPM [9, 14].

In adults, cIMT is considered a strong prognostic risk factor for cardiovascular disease. Children with CKD, especially CKD stage V, have significantly higher cIMT than the general population. HTN has been identified as an independent risk factor [25].

Taken together, these studies confirm that intermediate cardiovascular outcomes, such as LVH and increased cIMT, develop very early during CKD in children, becoming epidemic during ESRD, and that HTN is a strong risk factor for these abnormalities. The cumulative burden of HTN could be particularly dramatic in patients developing ESRD during childhood, who often experience recurrent cycles of dialysis and a long history of renal replacement therapy. It is therefore possible to argue that better management of BP should have a significant effect on short- and long-term cardiovascular outcomes of this population. Periodic monitoring of target organ damage, in particular, LVMI, is of utmost importance in the management of BP in children on dialysis. We suggest

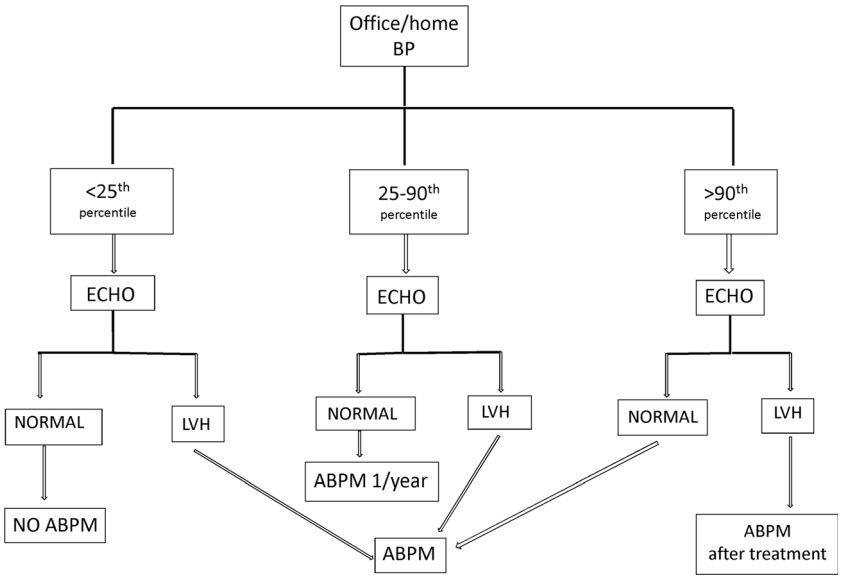

Fig. 1 Indications for ambulatory blood pressure monitoring in children on dialysis. *BP* blood pressure, echo echocardiography, *LVH* left ventricular hypertrophy, *ABPM* ambulatory blood pressure monitoring

performing echocardiography at least annually in all stable children on dialysis.

Target BP on treatment

Consensus on the recommended target for BP in children on dialysis has never been reached. Specific recommendations have only been proposed for children with CKD not on dialysis. The most recent guidelines are basically based on the results of the ESCAPE trial, which showed that an intensified BP control (target BP <50th percentile) leads to slower progression of CKD in children with CKD stages II–IV on fixed-dose ramipril treatment compared with the standard BP target (50th to 90th percentile) [26]. Based on this trial, the 2012 Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommended a systolic and diastolic BP target less than the 50th percentile for gender, age, and height in children with CKD stages II–IV [27].

Very few data exist for children maintained by dialysis. In a retrospective study of 87 pediatric patients on PD, loss of residual renal function was significantly higher in children with systolic and/or diastolic BP >95th percentile, whereas no significant differences were found in loss of residual renal function in children with BP <50th percentile, 50th–90th percentile, and 90th–95th percentile: the authors concluded that BP levels <50th percentile could be not superior to a target BP < 95th percentile in preserving residual kidney function in children on chronic PD [28]. Interestingly, no specific class of antihypertensive drugs was associated with a significant protective effect on residual renal function in children on dialysis. BP values within the normal range (<90th percentile) proved to be associated with improvement of LVMI in children on HD [24], thus suggesting that this threshold could be appropriate until more sound data are available.

Management of BP

Given the multifactorial nature of HTN in children with ESRD, a comprehensive approach to this problem should consider all the possible contributing factors, including the correction of hyperparathyroidism and, if possible, the tailoring or withdrawal of medications that predispose to HTN.

As Na and water overload is the main cause of HTN in children on dialysis, adequate volume control is a priority, and only when BP is not well controlled after achieving a stable volume, should antihypertensive medications be considered. The strategies to optimize BP in children on dialysis are summarized in Fig. 2.

Volume management in children on dialysis

Dry weight assessment

The first step towards obtaining adequate volume control in children on dialysis is the correct identification of dry weight (DW), which has traditionally been defined as the lowest tolerated post-dialysis body weight at which there are minimal signs or symptoms of hypo- or hypervolemia. A number of assessment methods for volume status have been described: clinical examination (weight, jugular venous distension, orthostatic vital signs, presence of edema), biochemical markers (serum proteins, atrial natriuretic peptide, and its second messenger cGMP, brain natriuretic peptide, troponin T), inferior vena cava diameter, continuous blood volume measurement in hemodialysis patients, numerous published equations to

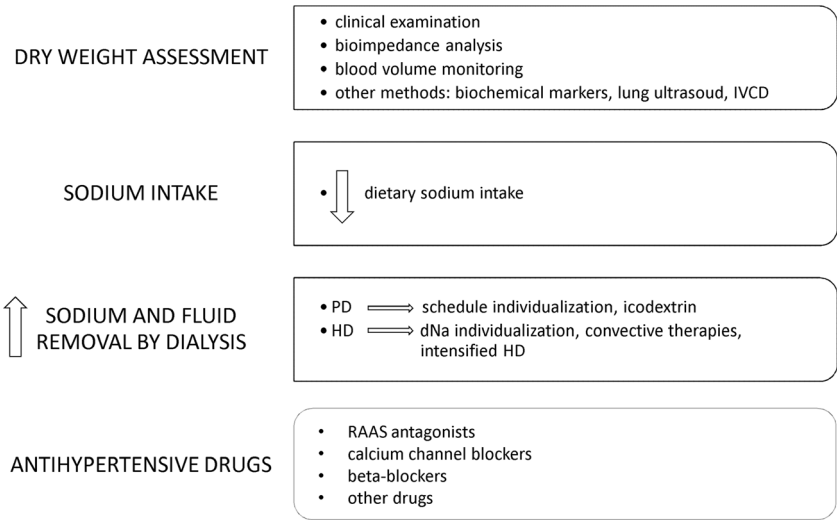

Fig. 2 Management of blood pressure in children on dialysis. *IVCD* inferior vena cava diameter, *PD* peritoneal dialysis, *HD* hemodialysis, *RAS* renin–angiotensin system

predict total body water using anthropometry, dilution techniques (deuterium, tritium, bromine), bioelectrical impedance analysis (BIA) and lung ultrasound. The consensus exists that clinical assessment of DW based on history and physical examination only is inaccurate, especially in a growing child. Dry weight is often identified on the basis of BP control, but this approach is misleading. Hypervolemia is not the only possible cause of HTN; thus, HTN does not necessarily mean volume overload. On the other hand, the presence of normal BP does not necessarily mean euvolemia, and volume overload can occur even with normal BP. Even in the case of true volume-dependent HTN, BP can normalize several months after DW has been achieved, which is known as the "lag phenomenon". The relationship between pre-HD BP and volume status was assessed in a recent study involving 23 children on HD [29]. This study evaluated 463 concomitant measurements of pre-HD BP and relative overhydration (relOH), assessed by bioimpedance spectroscopy. Hypertension was diagnosed in 39% of sessions, but relOH >7% was present in only 31% of them; in the same way, BP was normal in 61% of the sessions, but in 33% of them relOH was higher than 7% [29].

A DW prescription based on BP levels carries not only the risk of maintaining a status of chronic volume overload, but also the risk of aggressive and unjustified ultrafiltration. Recent evidence confirms the frequent occurrence of myocardial stunning during standard, well-tolerated, HD sessions in children [30]. Adult studies emphasize the burden of cardiac injury due to aggressive ultrafiltration, with the risk of myocardial hibernation, fibrosis, and increased cardiovascular events [30]. Moreover, hypovolemia secondary to excessive ultrafiltration can result in a loss of residual renal function, which has dramatic effects on metabolic control, fluid balance, and even growth.

Taking all these data into account, it is widely accepted that DW prescription should be based not only on a comprehensive assessment, including history, clinical signs, and BP levels, but also on some methods for fluid status assessment, such as BIA, lung ultrasound, and blood volume monitoring (BVM).

Both multi-frequency and single-frequency BIA have been proposed to assess DW in patients on dialysis [29, 31, 32]. The first approach has been used with good results in adult dialysis patients and a few reports show promising results in children [29], although a formal validation in pediatric patients is still lacking. Single-frequency BIA provides two parameters, resistance and reactance, which are expressions of tissue water content and tissue cell mass respectively. A recent study on 14 children on chronic HD showed that the percentage change in resistance during the HD session correlated directly with percentage body weight change and with percentage blood volume change, suggesting a possible role of this simple parameter in the assessment of DW [31]. In a single-center study on 31 children on chronic HD, a simple approach based on serial BIA measurements led to improved median LVMI, reduced LVH prevalence, and disappearance of pulmonary edema [32].

Lung ultrasound consists of the echographic measurement of the number of B-lines, which are hyperechogenic artifacts at the pleural line originating from the partial reflection of the ultrasound beam when lung density increases owing to congestion [33, 34]. A recent report on 23 children with acute kidney injury or ESRD demonstrated a significant correlation between the number of B-lines and the proportional increase in patient weight from the target weight [33]. When compared with other methods of DW assessment (clinical evaluation, BP measurement, BIA spectroscopy, and inferior vena cava diameter) in 13 children on dialysis, lung ultrasound was the only parameter that correlated significantly with volume overload [34].

Blood volume monitoring involves the optical or ultrasound assessment of serum hemoglobin or total protein to calculate the percentage change of blood volume during the

entire HD session. Several studies in adult and pediatric HD patients support the use of BVM to prevent intradialytic morbidity by identifying patients with volume overload [35–37]. Among them, Patel et al. assessed the usefulness of BVM in 20 HD children over a 6-month period: at the end of the study, they observed a significant increase in mean ultrafiltration, improvement in BP with fewer antihypertensive medications and a reduced incidence of intradialytic events [36]. The results of the most important studies focusing on the effect of BVM use on BP in children on HD are reported in Table 2.

Taken together, these data suggest that an improved assessment of DW, based not only on clinical parameters and BP, but also on some instrumental non-invasive tools, might lead to improved BP control and cardiovascular status of children on dialysis.

Reduction of dietary sodium intake

A second step toward improving volume management in children on dialysis is to reduce IDWG, which correlates significantly with BP and LVMI [11, 12].

High IDWG in patients on dialysis is mainly due to osmometric thirst secondary to salt ingestion, whereas other causes of thirst are negligible (social drinking, xerostomia due to medications, volumetric thirst at the end of dialysis): attempts at fluid restriction may be useless if Na intake is not restricted at the same time. It can be assumed that an anuric patient takes in approximately 1 l of water for every 8 g of salt consumed. Sodium balance has a negative impact on BP and cardiovascular status through several mechanisms other than volume expansion, such as increased total peripheral resistance, vascular smooth muscle cell hypertrophy, and reactive oxygen species promotion.

Some adult studies have demonstrated that a low Na diet may result in lower IDWG, lower intradialytic complications, better BP values, reduced LVMI, and lower mortality [38, 39].

Both the KDOQI and the KDIGO guidelines recommend restriction of Na intake for children with CKD who have HTN or pre-HTN, on the basis of the age-based recommended daily intake for healthy children [27, 40]: upper limits for Na intake are 1,500 mg/day for children aged 2–3 years, 1,900 mg/day for children aged 4–8 years, 2,200 mg/day for children and adolescents aged 9–13 years, and 2,300 mg/day for the population aged ≥14 years. In developed countries, 92–94% of healthy children aged 2–18 years exceeded current Na dietary recommendations [41]. Data from the CKiD Study showed that the median Na intake in children with CKD 2–4 was 3,089 mg/day, exceeding the recommended maximum daily intake for all age groups; in particular, more than 25% of adolescents consumed more than 5,150 mg of Na daily [42]. Looking at the sources of Na, it is well known that salt added by manufacturers during food processing accounts for almost 75% of the total Na intake in the general population, whereas 10% of intake is due to Na occurring naturally in food and salt added at the table or while cooking provides 5% and 10% of total intake respectively. Studies in industrialized countries show that the greatest contributors to Na intake in healthy children are cereals and cereal-based dishes (43%), followed

Table 2 Effect of blood volume monitoring on blood pressure (*BP*) in children on HD

Reference	N. patients	BP measurement method	Blood pressure	AntiHTN use	IntraHD events
Patel et al. [36]	20	24 h ABPM	Daytime SBP index: from 0.97 to 0.87 ($p = 0.05$) Daytime DBP index: from 0.94 to 0.79 ($p = 0.05$) Nighttime SBP index: from 1.04 to 0.95 ($p = 0.09$) Nighttime DBP index: from 1.02 to 0.88 ($p = 0.10$)	From 19/20 to 10/20 patients ($p = 0.04$)	In 8 patients with baseline events: from 26 events/week to 8 events/week ($p = 0.03$)
Candan et al. [35]	9	44 h ABPM	Mean SBP: from 129.3 to 122.6 mmHg ($p = 0.034$) Mean DBP: from 87.4 to 81.5 mmHg ($p = 0.050$) Mean SBP load: from 74.8% to 59.8% mmHg ($p = 0.036$) Mean DBP load: from 80.4% to 65.6% mmHg ($p = 0.063$)	From 9/9 to 4/9 patients	From 16% to 36% ($p = 0.098$)
Fadel et al. [37]	15	Casual pre- and post-HD BP	No significant differences for pre-HD or post-HD SBP and DBP	Not reported	From 33 to 4 episodes/180 sessions ($p = 0.04$)

ABPM ambulatory blood pressure monitoring, *AntiHTN* antihypertensive medications, *SBP* systolic blood pressure, *DBP* diastolic blood pressure

by meat (16%) and milk (16%) products and savory sauces and condiments (7%) [43].

Low compliance is the main limiting factor as regards the efficacy of a dietary approach to HTN in children. It is well demonstrated that salt exposure after the age of 2 years results in a predilection for salt in foods, and that salt sensing of the tongue is strictly dependent on the amount of Na ingested. As salt intake is reduced, adaptation of the taste receptors occurs over a period of some weeks or months, and salt-rich food tastes too salty afterwards; on the contrary, an occasional intake of salted food impedes adaptation to a salt-restricted diet, with salt-free food being perceived as tasteless. Twin studies confirm that environment plays a larger role than genetics in determining individual differences in recognition thresholds for saltiness [44]. Na consumption can therefore be considered an addiction and it should be treated accordingly: the hidden salt in industrial food and occasional exposure to salt are major obstacles in adapting to a low-salt diet.

As regards the hidden Na intake, some drugs contain a substantial amount of Na: for instance, 1 mg of Na per 1 g of powder is present in sodium polystyrene for the treatment of hyperkalemia. Na-free exchange resins should therefore be prescribed in hypertensive children.

An accurate dietary assessment performed by a dietician by means of a 3-day dietary diary is a powerful tool in the evaluation of Na intake. The family should be encouraged to use fresh food, to cook rice and pasta without salt, to use sauces as rarely as possible, to check nutritional information on food labels, and to look for low-Na alternatives. Personalized dietary counseling is a priority for children on dialysis, as is the support of a specialized dietician and the optimization of Na removal by dialysis.

Optimization of dialysis prescription

Sodium and water management during PD Sodium removal during PD is mainly due to the diffusive passage of Na through small pores, which is influenced by the transmembrane Na gradient (plasma–dialysate Na difference), peritoneal membrane integrity, and peritoneal area recruitment, which mainly depends on filling volume. To increase Na removal in PD, exchanges with long dwells and high volumes are needed: sodium removal increases with dwell volume, which may be increased up to 1,400 ml/m^2 body surface area in children >2 years and based on intraperitoneal pressure measurements [45]. The commercially available PD solutions contain 132 to 134 mmol/l of sodium; some adult studies showed that better Na removal could be achieved by reducing the dialysate sodium to 115–126 mmol/l and increasing glucose concentration to 2.5% to maintain osmolality [46].

Fluid transport across the peritoneal membrane occurs by means of a solute-free water transport through ultrasmall pores, driven by an osmotic gradient, and solute-coupled water transport, driven by an osmotic and hydrostatic pressure gradient. The major determinant of fluid removal is the osmotic gradient, usually driven by the glucose dialysate concentration, which is maximal in the early phase of the dwell. The intraperitoneal hydrostatic pressure is the second most important determinant of fluid removal and it correlates directly with the intraperitoneal volume [47, 48]. Optimization of water removal during PD is therefore obtained by means of short dwells and low intraperitoneal volumes, the opposite for Na removal [45]. Possible alternatives are the use of icodextrin and higher a dialysate glucose concentration, with its potential toxicity. Icodextrin is a solution of glucose polymers, which exert osmotic pressure across the peritoneal membrane. Pediatric studies showed that a linear increase in ultrafiltration could be obtained up to 8 h of dwell by using icodextrin, and that the larger the fill volume the higher the likelihood of achieving ultrafiltration [49].

To improve both Na and water removal, adapted automated PD has been proposed [50–53]. It consists of a couple of short dwell/small volume exchanges to improve ultrafiltration, followed by exchanges with longer dwell time and larger fill volume to promote toxins and Na removal [53]. This approach was tested in a multicenter prospective randomized crossover trial in 19 adults [53], who were treated with either adapted PD or conventional PD (45 days for each phase, with the same total amount of dialysate and duration). Compared with conventional PD, adapted PD resulted in significantly increased Na removal per session, increased ultrafiltration and, more importantly, better systolic and diastolic BP values [53]. The beneficial effect of adapted PD was also shown in a pediatric study over 20 years ago and confirmed in a recent crossover study in 4 children that demonstrated a dramatic improvement of Na extraction (169%) and ultrafiltration (128%) with adapted PD compared with conventional PD [50, 51]. However, a computer simulation using the three-pore model showed a very small improvement in ultrafiltration and Na removal in adapted PD compared with conventional PD, indicating the need for accurate sodium determination [52].

Sodium and water management during HD Sodium removal during HD is mainly driven by convection (approximately 80%) through ultrafiltration, whereas removal by diffusion is often negligible (around 20%) and depends on the transmembrane Na gradient. Dialysate Na is usually set at 138–140 mEq/l, but pediatric data show high intra- and inter-patient pre-HD plasma Na level variability, often with values below 138 mEq/L.

Several adult studies have demonstrated the potential benefits of lower dialysate Na concentration on thirst, IDWG, and BP [54, 55]. Among others, Thein et al. obtained a significant reduction of BP, particularly in patients with the highest BP, after decreasing dialysate Na concentration from 141 to 138 mEq/L over a period of 8 months in 52 patients [54]. In

a small pediatric study of 480 HD sessions in 5 children, a reduction of dialysate Na from 140 to 138 mEq/l was associated with lower IDWG and improved pre-HD systolic and diastolic BP (from 133 to 127 and from 84 to 73 mmHg respectively) [56]. On the other hand, some studies reported an increased incidence of intradialytic hypotension and a need for saline infusion in adults treated with a lower dialysate Na concentration [55]. An individualized Na prescription, which would take into account the patient pre-HD plasma Na, IDWG, BP values, and intra-HD hemodynamic stability, has been advocated and the benefits of a personalized approach have been highlighted by some adult studies. However, the high variability of plasma Na makes this approach difficult to implement in clinical practice [29].

Adult randomized controlled studies showed that high volume on-line hemodiafiltration (HDF) is associated with improved overall survival in comparison with standard HD, resulting predominantly from a lower cardiovascular mortality, possibly because of the better preservation of left ventricular mass and function. Among the possible beneficial effects, high volume HDF was associated with a significant reduction of intra-dialytic hypotension. The effect of convective therapies on sodium removal are still debated: some adult studies have demonstrated a greater reduction of serum sodium concentration after HDF than after standard high-flux HD, with a significant correlation between the change in serum Na and systolic BP [57]. Pediatric data are still lacking.

Several adult studies and some pediatric reports have clearly demonstrated that the best strategy for the optimization of Na and fluid management in HD patients is intensified HD, which is daily, home or nocturnal HD or hemodiafiltration (HDF) [58–62]. In a single-centre prospective trial five oligo-anuric children were switched from standard thrice-weekly HDF to daily on-line HDF (3 h, six times/week) [58]. At 6 and 12 months, the authors observed a significant improvement in BP (from a mean BP of 95 to 82 mmHg), allowing for the withdrawal of antihypertensive medications in 4 out of 5 children, a reduction of LVH, and a significant increase in left ventricular systolic function [58]. In a 16-week single-center study, 4 children were converted to the six-times-weekly HD using the NxStage™ system: a significant reduction in 24 h ABPM mean systolic (−9.2 mmHg) and diastolic (−8.5 mmHg) BP values was observed [59]. A significant improvement in BP with reduction of antihypertensive medications was also observed during hospital-based intermittent nocturnal 8 h HD or HDF (three times/week) [60–62]. Recently, Thumfart et al. compared 13 children on intermittent nocturnal HD with 13 children on PD over a 6-month period: only those on HD showed a significant improvement in BP and the disappearance of LVH [62]. A summary of the results obtained with intensified HD in children is shown in Table 3.

These data clearly suggest that intensified HD/HDF regimens represent the best strategy for the normalization of BP and the reduction of target organ damage in children on dialysis. Moreover, several other beneficial effects have been reported, such as improved growth, better metabolic control, no need for a strict diet, free fluid intake, reduced medication burden, improvement in general well-being, better dialysis acceptance, and an improved quality of life.

Anti-hypertensive medications

Given how difficult it is to manage fluid status in children on dialysis, it is not surprising that most pediatric patients maintained by dialysis receive antihypertensive drugs: 58–63% of children on HD and 52–55% of those on PD (Table 1) [6–8].

Trials demonstrating the superiority of a particular class of drugs over another are lacking in children on dialysis, with studies limited to CKD stages 2–4. In a cross-sectional analysis of the CKiD study, uncontrolled BP was significantly associated with the use of antihypertensive medication other than angiotensin-converting enzyme inhibitors (ACE-Is) or angiotensin receptor blockers (ARBs) [63]. A prospective analysis of the same cohort of 478 children with CKD stages 2–4 concluded that the use of BP-lowering agents other than antagonists of the renin–angiotensin system (RAS) was a significant predictor of LVH, whereas both ACE-Is and ARBs seemed to be protective for the development of LVH, although not significantly [64]. The IPPN registry showed that, among 507 children on PD, concentric LVH was less common in patients treated with RAS antagonists than in those not receiving this class of drugs [5].

All guidelines recommend ACE-Is or ARBs as first-line antihypertensive agents for children with CKD [27, 40]. Even if specific recommendations are not available for children on dialysis, it seems reasonable to suggest RAS antagonists as the first-line anti-hypertensive agents in children on dialysis too. These drugs are usually well-tolerated in children on dialysis. Some adult studies showed an increased risk of hyperkalemia in patients on HD treated with ACE-Is, probably because of the inhibited extrarenal potassium loss, not confirmed by other trials. A practitioner survey on the use of BP-lowering agents in children maintained by dialysis showed that dihydropyridine calcium channel blockers represented the first choice for 65.8% and 57% of respondents for HD and PD patients respectively, followed by ACE-I (44.6% in HD, 44.3% in PD) [65]. The preference for this class of drugs is probably due to their optimal safety profile.

When using an antihypertensive agent in patients on dialysis, some pharmacokinetic aspects should be taken into account as regards urine excretion and removal by

Table 3 Effect of intensified hemodialysis/hemodiafiltration on blood pressure

Reference	Number of patients	HD schedule	Duration (months)	BP	AntiHTN drugs
Fischbach et al. [47]	5	3 h × 6/week In-center HDF	12	Mean BP: 95 mmHg at baseline 82 mmHg at 6 months ($p < 0.05$) 87 mmHg at 12 months ($p < 0.05$)	From 5/5 to 1/5
Goldstein et al. [59]	4	6/week HD (3 home HD)	16	Mean SBP: −9.25 mmHg Mean DBP: −8.75 mmHg Mean SBP load: −13.4% Mean DBP load: −20.0%	From 2/4 to 0/4
Hoppe et al. [60]	16	8 h × 3/week In-center NHD	7	Pre-HD mean BP from 102.3 to 93 mmHg	From 3 to 1.5 drugs/patient /day
Thumfart et al. [61]	7	8 h × 3/week In-center nocturnal HDF or NHD	3	Pre-HD mean BP 8 mmHg lower with nocturnal HDF and nocturnal HD than with standard HD ($p < 0.001$)	From 7/7 to 2/7
Thumfart et al. [62]	13	8 h × 3/week In-center NHD vs 13 PD patients	6	Mean BP – 6 mmHg in NHD vs + 1 mmHg in PD	3/13 NHD vs 10/13 PD

HD bicarbonate HD, *HDF* hemodiafiltration, *NHD* nocturnal hemodialysis, *PD* peritoneal dialysis, *SBP* systolic blood pressure, *DBP* diastolic blood pressure

dialysis. ACE-Is are largely removed by HD (i.e., ramipril is removed by 20–30%, enalapril by 35–50%), with the exception of fosinopril, whereas ARBs and calcium channel blockers are not cleared by HD. Among beta-blockers, water-soluble versions such as atenolol and metoprolol are highly dialyzable (75% and 50% respectively), whereas combined α- and β-blockers (labetalol, carvedilol) are not affected by the treatment. Some drugs can be administered three times per week, at the end of the HD session, with a clear benefit for noncompliant patients. In particular, some adult studies actually showed that a significant BP reduction could be obtained with thrice-weekly dosing of atenolol or lisinopril. Removal by PD is usually considered to be negligible for most of the drugs.

In clinical practice, there is a marked heterogeneity as far as the timing of antihypertensive prescription is concerned: 66.7% of respondents of the aforementioned survey recommended holding BP-lowering agents on the morning of scheduled HD days and 14% avoided certain types of medications in the evening for patients on nocturnal PD [65]. As a general rule, the practice of routinely avoiding antihypertensive drugs before the HD session could have potential consequences, such as intra-HD hypertension, poorer BP control, and arrhythmias. For patients at risk for intra-HD hypotension, dialyzable agents such as ACE-Is (with the exception of fosinopril) are preferable. For these patients, and particularly when nocturnal dipping is reduced, nocturnal administration could be an optimal solution. Patients with intra-HD HTN should be treated with non-dialyzable agents administered before the HD treatment, such as ARBs and some beta-blockers.

Conclusions

Concrete evidence highlights the role of HTN in producing major cardiovascular complications, in particular LVH and increased cIMT, in children on dialysis. A few strategies for achieving satisfactory BP control have proved effective in pediatric studies: on the one hand, careful BP evaluation by means of ABPM and an accurate DW assessment through BIA, lung ultrasound, and BVM; on the other, a reduction of sodium overload through dietary intervention, reduced dialysate sodium prescription and intensified HD/HDF schedules.

Unfortunately, BP remains poorly controlled in most children with ESRD. Further studies are needed to improve strategies for lowering BP and protecting these patients from short- and long-term cardiovascular complications and death.

Key summary points

1. Hypertension is very common in children on dialysis and is associated with left ventricular hypertrophy and increased carotid intima-media thickness
2. The gold-standard for BP assessment in children with ESRD is ABPM
3. Avoiding volume and salt overload is the most important step in optimizing BP control in children on dialysis, which can be obtained through an accurate assessment of dry weight, reduction of dietary sodium intake,

avoidance of sodium load by dialysis, and intensified dialysis regimens
4. To prescribe antihypertensive medications appropriately, the specific pharmacokinetic characteristics of each drug should be taken into account

Multiple choice questions (answers are provided after the reference section)

1. Which of the following methods for dry weight assessment is associated with better BP control in children on hemodialysis?
   a) Brain natriuretic peptide
   b) Inferior vena cava diameter
   c) Blood volume monitoring
   d) Lung ultrasound
   e) All the above

2. The most important source of dietary sodium in children is:
   a) Salt added to the food during processing
   b) Salt added while cooking
   c) Salt added at the table
   d) Sodium occurring naturally in food
   e) All the above in the same amount

3. Sodium removal during peritoneal dialysis can be maximized by:
   a) Decreasing dwell time
   b) Reducing dwell numbers
   c) Increasing dwell volume
   d) Reducing dwell volume
   e) Volumes and dwells do not affect sodium removal during peritoneal dialysis

4. Improvement of blood pressure in pediatric studies on children treated with dialysis has been obtained by means of:
   a) Reduction of dialysate sodium concentration
   b) Daily hemodiafiltration
   c) Nocturnal hemodialysis
   d) Nocturnal hemodiafiltration
   e) All the above

5. Which of the following drugs is removed by hemodialysis?
   a) Carvedilol
   b) Calcium channel blockers
   c) Angiotensin receptor blockers
   d) Atenolol
   e) Labetalol

Compliance with ethical standards

Financial disclosure statement Nothing to disclose.

Conflicts of interest None to declare.

References

1. Kramer A, Stel VS, Tizard J, Verrina E, Ronnholm K, Palsson R, Maxwell H, Jager KJ (2009) Characteristics and survival of young adults who started renal replacement therapy during childhood. Nephrol Dial Transplant 24:926–933
2. Chesnaye NC, Schaefer F, Groothoff JW, Bonthuis M, Reusz G, Heaf JG, Lewis M, Maurer E, Paripović D, Zagozdzon I, van Stralen KJ, Jager KJ (2016) Mortality risk in European children with end-stage renal disease on dialysis. Kidney Int 89:1355–1362
3. US Renal Data System: USRDS 2015 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States, Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2015
4. Mitsnefes MM, Daniels SR, Schwartz SM, Khoury P, Strife CF (2001) Changes in left ventricular mass in children and adolescents during chronic dialysis. Pediatr Nephrol 16:318–323
5. Bakkaloglu SA, Borzych D, Soo Ha I, Serdaroglu E, Büscher R, Salas P, Patel H, Drozdz D, Vondrak K, Watanabe A, Villagra J, Yavascan O, Valenzuela M, Gipson D, Ng KH, Warady BA, Schaefer F, International Pediatric Peritoneal Dialysis Network (2011) Cardiac geometry in children receiving chronic peritoneal dialysis: findings from the International pediatric peritoneal dialysis Network (IPPN) registry. Clin J Am Soc Nephrol 6:1926–1933
6. Chavers BM, Solid CA, Daniels FX, Chen SC, Collins AJ, Frankenfield DL, Herzog CA, Haskin O, Wong CJ, McCabe L, Begin B, Sutherland SM, Chaudhuri A (2009) Hypertension in pediatric long- term hemodialysis patients in the United States. Clin J Am Soc Nephrol 4:1363–1369
7. Kramer AM, van Stralen KJ, Jager KJ, Schaefer F, Verrina E, Seeman T, Lewis MA, Boehm M, Simonetti GD, Novljan G, Groothoff J (2011) Demographics of blood pressure and hypertension in children on renal replacement therapy in Europe. Kidney Int 80:1092–1098
8. Halbach SM, Martz K, Mattoo T, Flynn J (2012) Predictors of blood pressure and its control in pediatric patients receiving dialysis. J Pediatr 160:621–625
9. Chaudhuri A, Sutherland SM, Begin B, Salsbery K, McCabe L, Potter D, Alexander SR, Wong CJ (2011) Role of twenty-four-hour ambulatory blood pressure monitoring in children on dialysis. Clin J Am Soc Nephrol 6:870–876
10. Goldstein SL, Smith CM, Currier H (2003) Noninvasive interventions to decrease hospitalization and associated costs for pediatric patients receiving hemodialysis. J Am Soc Nephrol 14:2127–2131
11. Ozkahya M, Ok E, Toz H, Asci G, Duman S, Basci A, Kose T, Dorhout Mees EJ (2006) Long-term survival rates in haemodialysis patients treated with strict volume control. Nephrol Dial Transplant 21:3506–3513
12. VanDeVoorde RG, Barletta GM, Chand DH, Dresner IG, Lane J, Leiser J, Lin JJ, Pan CG, Patel H, Valentini RP, Mitsnefes MM (2007) Blood pressure control in pediatric hemodialysis: the Midwest pediatric Nephrology consortium study. Pediatr Nephrol 22:547–553
13. Paglialonga F, Consolo S, Galli MA, Testa S, Edefonti A (2015) Interdialytic weight gain in oligoanuric children and adolescents on chronic haemodialysis. Pediatr Nephrol 30:999–1005

14. Haskin O, Wong CJ, McCabe L, Begin B, Sutherland SM, Chaudhuri A (2015) 44-h ambulatory blood pressure monitoring: revealing the true burden of hypertension in pediatric hemodialysis patients. Pediatr Nephrol 30:653–660
15. Tkaczyk M, Nowicki M, Bałasz-Chmielewska I, Boguszewska-Bączkowska H, Drozdz D, Kołłataj B, Jarmoliński T, Jobs K, Kiliś-Pstrusińska K, Leszczyńska B, Makulska I, Runowski D, Stankiewicz R, Szczepańska M, Wierciński R, Grenda R, Kanik A, Pietrzyk JA, Roszkowska-Blaim M, Szprynger K, Zachwieja J, Zajaczkowska MM, Zoch-Zwierz W, Zwolińska D, Zurowska A (2006) Hypertension in dialysed children: the prevalence and therapeutic approach in Poland—a nationwide survey. Nephrol Dial Transplant 21:736–724
16. Van Buren PN, Inrig JK (2012) Hypertension and hemodialysis: pathophysiology and outcomes in adult and pediatric populations. Pediatr Nephrol 27:339–350
17. Hadtstein C, Schaefer F (2008) Hypertension in children with chronic kidney disease: pathophysiology and management. Pediatr Nephrol 23:363–371
18. Agarwal R, Andersen MJ, Bishu K, Saha C (2006) Home blood pressure monitoring improves the diagnosis of hypertension in hemodialysis patients. Kidney Int 69:900–906
19. Agarwal R, Brim NJ, Mahenthiran J, Andersen MJ, Saha C (2006) Out-of-hemodialysis-unit blood pressure is a superior determinant of left ventricular hypertrophy. Hypertension 47:62–68
20. Mitsnefes M, Flynn J, Cohn S, Samuels J, Blydt-Hansen T, Saland J, Kimball T, Furth S, Warady G, CKiD Study Group (2010) Masked hypertension associates with left ventricular hypertrophy in children with CKD. J Am Soc Nephrol 21:137–144
21. Barletta GM, Flynn J, Mitsnefes M, Samuels J, Friedman LA, Ng D, Cox C, Poffenbarger T, Warady B, Furth S (2014) Heart rate and blood pressure variability in children with chronic kidney disease: a report from the CKiD study. Pediatr Nephrol 29:1059–1065
22. Mitsnefes MM, Pierce C, Flynn J, Samuels J, Dionne J, Furth S, Warady B, CKiD study group (2016) Can office blood pressure readings predict masked hypertension? Pediatr Nephrol 31:163–166
23. Wühl E, Witte K, Soergel M, Mehls O, Schaefer F, German Working Group on Pediatric Hypertension (2002) Distribution of 24-h ambulatory blood pressure in children: normalized reference values and role of body dimensions. J Hypertens 20:1995–2007
24. Ulinski T, Genty J, Viau C, Tillous-Borde I, Deschênes G (2006) Reduction of left ventricular hypertrophy in children undergoing hemodialysis. Pediatr Nephrol 21:1171–1178
25. Litwin M, Wühl E, Jourdan C, Trelewicz J, Niemirska A, Fahr K, Jobs K, Grenda R, Wawer ZT, Rajszys P, Tröger J, Mehls O, Schaefer F (2005) Altered morphologic properties of large arteries in children with chronic renal failure and after renal transplantation. J Am Soc Nephrol 16:1494–1500
26. The ESCAPE Trial Group (2009) Strict blood-pressure control and progression of renal failure in children. N Engl J Med 361:1639–1650
27. Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group (2012) KDIGO clinical practice guideline for the management of blood pressure in chronic kidney disease. Kidney Int Suppl 2:337–414
28. Roszkowska-Blaim M, Skrzypczyk P, Jander A, Tkaczyk M, Bałasz-Chmielewska I, Żurowska A, Drożdż D, Pietrzyk JA (2015) Effect of hypertension and antihypertensive medications on residual renal function in children treated with chronic peritoneal dialysis. Adv Med Sci 60:18–24
29. Zaloszyc A, Schaefer B, Schaefer F, Krid S, Salomon R, Niaudet P, Schmitt CP, Fischbach M (2013) Hydration measurement by bioimpedance spectroscopy and blood pressure management in children on hemodialysis. Pediatr Nephrol 28:2169–2177
30. Hothi DK, Rees L, Marek J, Burton J, McIntyre CW (2009) Pediatric myocardial stunning underscores the cardiac toxicity of conventional hemodialysis treatments. Clin J Am Soc Nephrol 4:790–797
31. Oh G, Wong C, Begin B, Salsbery K, Sutherland S, Chaudhuri A (2014) Whole-body single-frequency bioimpedance analysis in pediatric hemodialysis patients. Pediatr Nephrol 29:1417–1423
32. Paglialonga F, Ardissino G, Galli MA, Scarfia RV, Testa S, Edefonti A (2012) Bioimpedance analysis and cardiovascular status in pediatric patients on chronic hemodialysis. Hemodial Int 16:S20–S25
33. Allinovi M, Saleem M, Romagnani P, Nazerian P, Hayes W (2016) Lung ultrasound: a novel technique for detecting fluid overload in children on dialysis. Nephrol Dial Transplant. doi:10.1093/ndt/gfw037
34. Allinovi M, Saleem MA, Burgess O, Armstrong C, Hayes W (2016) Finding covert fluid: methods for detecting volume overload in children on dialysis. Pediatr Nephrol 31:2327–2335
35. Candan C, Sever L, Civilibal M, Caliskan S, Arisoy N (2009) Blood volume monitoring to adjust dry weight in hypertensive pediatric hemodialysis patients. Pediatr Nephrol 24:581–587
36. Patel HP, Goldstein SL, Mahan JD, Smith B, Fried CB, Currier H, Flynn JT (2007) A standard, noninvasive monitoring of hematocrit algorithm improves blood pressure control in pediatric hemodialysis patients. Clin J Am Soc Nephrol 2:252–257
37. Fadel FI, Makar SH, Eskander AE, Aon AH (2014) Decreasing intra-dialytic morbid events and assessment of dry weight in children on chronic hemodialysis using non-invasive changes in hematocrit. Saudi J Kidney Dis Transpl 25:1030–1037
38. Kayikcioglu M, Tumuklu M, Ozkahya M, Ozdogan O, Asci G, Duman S, Toz H, Can LH, Basci A, Ok E (2009) The benefit of salt restriction in the treatment of end-stage renal disease by haemodialysis. Nephrol Dial Transplant 24:956–962
39. McCausland FR, Waikar SS, Brunelli SM (2012) Increased dietary sodium is independently associated with greater mortality among prevalent hemodialysis patients. Kidney Int 82:204–211
40. National Kidney Foundation (2004) K/DOQI clinical practice guidelines on hypertension and antihypertensive agents in chronic kidney disease. Am J Kidney Dis 43:S1–S290
41. Jackson SL, King SM, Zhao L, Cogswell ME (2016) Prevalence of excess sodium intake in the United States—NHANES, 2009–2012. MMWR Morb Mortal Wkly Rep 64:1393–1397
42. Hui WF, Betoko A, Savant JD, Abraham AG, Greenbaum LA, Warady B, Moxey-Mims MM, Furth SL (2016) Assessment of dietary intake of children with chronic kidney disease. Pediatr Nephrol. doi:10.1007/s00467-016-3491-5
43. Grimes CA, Campbell KJ, Riddell LJ, Nowson CA (2011) Sources of sodium in Australian children's diets and the effect of the application of sodium targets to food products to reduce sodium intake. Br J Nutr 105:468–477
44. Wise PM, Hansen JL, Reed DR, Breslin PA (2007) Twin study of the heritability of recognition thresholds for sour and salty taste. Chem Senses 32:749–754
45. Fischbach M, Schmitt CP, Shroff R, Zaloszyc A, Warady BA (2016) Increasing sodium removal on peritoneal dialysis: applying dialysis mechanics to the peritoneal dialysis prescription. Kidney Int 89:761–766
46. Davies D, Carlsson O, Simonsen O, Johansson AC, Venturoli D, Ledebo I, Wieslander A, Chan C, Rippe B (2009) The effects of low-sodium peritoneal dialysis fluids on blood pressure, thirst and volume status. Nephrol Dial Transplant 24:1609–1617
47. Fischbach M, Terzic J, Laugel V, Escande B, Dangelser C, Helmstetter A (2003) Measurement of hydrostatic intraperitoneal pressure: a useful tool for the improvement of dialysis dose prescription. Pediatr Nephrol 18:976–980
48. Fischbach M, Terzic J, Becmeur F, Lahlou A, Desprez P, Battouche D, Geisert J (1996) Relationship between intraperitoneal

hydrostatic pressure and dialysate volume in children on PD. Adv Perit Dial 12:330–334
49. Rousso S, Banh TM, Ackerman S, Piva E, Licht C, Harvey EA (2016) Impact of fill volume on ultrafiltration with icodextrin in children on chronic peritoneal dialysis. Pediatr Nephrol 31:1673–1679
50. Fischbach M, Desprez P, Donnars F, Hamel G, Geisert J (1994) Optimization of CCPD prescription in children using peritoneal equilibration test. Adv Perit Dial 10:307–309
51. Zaloszyc A, Schmitt CP, Schaefer B, Doutey A, Terzic J, Menouer S, Higel L, Fischbach M (2016) Peritoneal equilibration test: conventional versus adapted. Preliminary study. Nephrol Ther. doi:10.1016/j.nephro.2016.07.444
52. Rippe B, Öberg CM (2016) Is adapted APD theoretically more efficient than conventional APD? Perit Dial Int. doi:10.3747/pdi.2015.00144
53. Fischbach M, Issad B, Dubois V, Taamma R (2011) The beneficial influence on the effectiveness of automated peritoneal dialysis of varying the dwell time (short/long) and fill volume (small/large): a randomized controlled trial. Perit Dial Int 31:450–458
54. Thein H, Haloob I, Marshall MR (2007) Associations of a facility level decrease in dialysate sodium concentration with blood pressure and interdialytic weight gain. Nephrol Dial Transplant 22:2630–2639
55. Munoz Mendoza J, Arramreddy R, Schiller B (2015) Dialysate sodium: choosing the optimal hemodialysis bath. Am J Kidney Dis 66:710–720
56. Marsenic O, Anderson M, Couloures KG, Hong WS, Kevin Hall E, Dahl N (2016) Effect of the decrease in dialysate sodium in pediatric patients on chronic hemodialysis. Hemodial Int 20:277–285
57. Hwang KS, Choi EY, Park JS, Lee CH, Kang CM, Kim GH (2013) Postdialysis serum sodium changes and systolic blood pressure in patients undergoing online hemodiafiltration and high-flux hemodialysis. Kidney Res Clin Pract 32:62–65
58. Fischbach M, Terzic J, Laugel V, Dheu C, Menouer S, Helms P, Livolsi A (2004) Daily on-line haemodiafiltration: a pilot trial in children. Nephrol Dial Transplant 19:2360–2367
59. Goldstein SL, Silverstein DM, Leung JC, Feig DI, Soletsky B, Knight C, Warady BA (2008) Frequent hemodialysis with NxStage system in pediatric patients receiving maintenance hemodialysis. Pediatr Nephrol 23:129–135
60. Hoppe A, von Puttkamer C, Linke U, Kahler C, Booss M, Braunauer-Kolberg R, Hofmann K, Joachimsky P, Hirte I, Schley S, Utsch B, Thumfart J, Briese S, Gellermann J, Zimmering M, Querfeld U, Muller D (2011) A hospital-based intermittent nocturnal hemodialysis program for children and adolescents. J Pediatr 158:95–99
61. Thumfart J, Puttkamer CV, Wagner S, Querfeld U, Müller D (2014) Hemodiafiltration in a pediatric nocturnal dialysis program. Pediatr Nephrol 29:1411–1416
62. Thumfart J, Hilliger T, Stiny C, Wagner S, Querfeld U, Müller D (2015) Is peritoneal dialysis still an equal option? Results of the Berlin Pediatric Nocturnal Dialysis Program. Pediatr Nephrol 30:1181–1187
63. Flynn JT, Mitsnefes M, Pierce C, Cole SR, Parekh RS, Furth SL, Warady BA, Chronic Kidney Disease in Children Study Group (2008) Blood pressure in children with chronic kidney disease: a report from the chronic kidney disease in children study. Hypertension 52:631–637
64. Kupferman JC, Aronson Friedman L, Cox C, Flynn J, Furth S, Warady B, Mitsnefes M, CKiD Study Group (2014) BP control and left ventricular hypertrophy regression in children with CKD. J Am Soc Nephrol 25:167–174
65. Lin JJ, Mitsnefes MM, Smoyer WE, Valentini RP (2009) Antihypertensive prescription in pediatric dialysis: a practitioner survey by the Midwest pediatric Nephrology consortium study. Hemodial Int 13:307–315

Answers to questions

1. c; 2. a; 3. c; 4. e; 5. d