By Jula K. Inrig and Kevin Griffiths

In this month’s issue, Jula K. Inrig of the ASN Dialysis Advisory Group and Kevin Griffiths of the ASN Practicing Nephrologists Advisory Group converse about how to handle hypertension in the dialysis unit and about blood pressure goals for patients.

Practice Pointers

Hypertension and Blood Pressure Goals in the Dialysis Unit

Intradialytic hypertension corresponds with improvements in SBP. A recent uncontrolled study of 25 patients with intradialytic hypertension demonstrated that the use of carvedilol (at doses up to 50 mg twice daily) abrogated the intradialytic rise in BP among two-thirds of these patients. The improvement in intradialytic hypertension corresponded with improvements in endothelial cell function. Although RCTs are needed to confirm this, carvedilol is certainly a good option for BP control among those who do not improve with dry weight reduction.

Two potential dialysis alterations have been suggested to help control BP among those with intradialytic hypertension: lowering dialysate calcium (by stabilizing nitric oxide and endothelin-1 release) and lowering dialysate calcium (by reducing cardiac contractility). Both measures have been tested in early stages and have been promising.

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JKI: Please tell us about intradialytic hypertension. Why is it so difficult to define it? What are the proposed mechanisms?

Clinically, intradialytic hypertension is defined as a rise in blood pressure (BP) that occurs during dialysis; you tend to recognize it when you see it (or get called by the nurse about it).

In research, most studies define intradialytic hypertension based on an increase in BP occurring from before to after dialysis, using systolic BP (SBP), mean arterial pressure, or both. However, research definitions of intradialytic hypertension do not always take into consideration measurements made during dialysis, because these are not always readily available, and these more modest increases in BP may be less recognized by clinicians.

Proposed mechanisms for intradialytic hypertension include volume overload, sodium excess, excess endothelin-1 relative to nitric oxide, sympathetic overactivity, dialyzability of medications, and overactivity of the renin-angiotensin-aldosterone system. Evidence suggests that intradialytic hypertension is caused by an imbalance in vasoregulators endothelin-1 and nitric oxide. What causes that imbalance is yet to be determined.

JKI: What is the clinical significance of BP increases during dialysis? Prevalence, morbidity and mortality, outcomes data, and so on? Is there any correlation between intradialytic hypertension and dialysis adequacy?

An increase in SBP above 10 mm Hg from before to after dialysis has been associated with increased hospitalizations and higher mortality. However, evolving research suggests that even small increases in BP may be less recognized by clinicians.

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JKI: How effective is dry weight reduction alone in controlling BP in patients receiving conventional thrice-weekly hemodialysis?

Solid evidence to support dry weight reduction for short-term control of BP comes from the Dry-Weight Reduction in Hypertensive HD Patients (DRIP) study. In this 8-week study, systematically lowering dry weight reduced ambulatory BP by an additional 7 mm Hg beyond usual care. However, these patients still required antihypertensive therapy and were not normotensive at the end of the study. Although achieving euvoolemia is very important for BP control and cardiovascular protection, thrice-weekly dialysis is not typically adequate for controlling BP.

JKI: What therapies (e.g., dialysis prescription alterations) can be used to treat a patient who experiences a hypertensive episode during dialysis? What role do dialysate sodium and dialysate calcium have in BP control?

Dry weight reduction should be tried before other therapies. However, I have not found this to be very effective among patients with persistent intradialytic increases in BP. A recent uncontrolled study of 25 patients with intradialytic hypertension demonstrated that the use of carvedilol (at doses up to 50 mg twice daily) abrogated the intradialytic rise in BP among two-thirds of these patients. The improvement in intradialytic hypertension corresponded with improvements in endothelial cell function. Although RCTs are needed to confirm this, carvedilol is certainly a good option for BP control among those who do not improve with dry weight reduction.

Two potential dialysis alterations have been suggested to help control BP among those with intradialytic hypertension: lowering dialysate calcium (by stabilizing nitric oxide and endothelin-1 release) and lowering dialysate calcium (by reducing cardiac contractility). Both measures have been tested in early stages and have been promising.

JKI: Is there any evidence pointing to different BP goals for young and old dialysis patients?

The current Kidney Disease Outcome Quality Initiative guidelines recommend a predialysis target BP value of less than 140/90 mm Hg and a postdialysis value of less than 130/80 mm Hg for either hemodialysis or peritoneal dialysis patients. However, a dialysis patient’s age may alter these parameters. Recent evidence suggests that dialysis patients over age 50 with SBP under 140 mm Hg have a higher mortality rate than do patients with SBP greater than 160 mm Hg. Dialysis patients under age 50 whose SBP is under 140 mm Hg had a lower mortality rate than when their SBP was above 160 mm Hg.

KG: Are there any studies that examine the use of predialysis or postdialysis BP or other BP measurements as guides to manage therapy? Is there any role for ambulatory BP monitoring in dialysis patients?

Predialysis and postdialysis BP readings are unreliable measurements on which to base antihypertensive therapy. Evidence suggests that predialysis SBP readings overestimate SBP by 10 mm Hg, whereas postdialysis SBP may underestimate SBP by 7 mm Hg. An ongoing pilot randomized controlled trial (RCT) is being conducted (BP in Dialysis, BID) to determine the safety and feasibility of targeting different predialysis BP levels.

Ambulatory BP monitoring and home BP readings are effective tools to guide therapy for dialysis patients because both are more reflective of true BP burden and have stronger relationships with adverse outcomes. These tools are particularly useful for patients who have large variability in dialysis unit BP measurements or discrepancies between home and dialysis unit readings. Thus, they can be used to help minimize overdosing or underdosing of antihypertensive medications.

KG: Are there preferred BP medications for hemodialysis or peritoneal dialysis patients, considering their specific characteristics, as well as dialyzability?

Angiotensin II receptor antagonists or ACE inhibitors, β-blockers, and calcium channel blockers are recommended as first-choice drugs depending on the patient’s other comorbidities. Peritoneal dialysis patients who have residual renal function (RRF) and hemodialysis patients with RRF benefit most from ACE inhibitors because this class regresses LVH and preserves RRF. Carvedilol or another β-blocker is recommended for patients who have had a recent heart attack and for those with systolic heart failure. Finally, evidence shows that diuretics are associated with preservation of RRF and lower all-cause mortality. Most ACE-I agents are dialyzable (except fosinopril), but angiotensin-receptor blockers, calcium channel blockers, and combination α-β-blockers are not dialyzable and should be preferred for those with high BP during hemodialysis.

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High dietary sodium intake increases thirst, interdialytic weight gain, and BP. Thus, dietary sodium restriction is very important for BP control among dialysis patients, particularly for those receiving conventional thrice-weekly dialysis. Small studies also suggest that lowering dialysate sodium may help control interdialytic BP. Several nonpharmacologic interventions are being tested in phase II and phase III trials among patients with resistant hypertension, including renal denervation and baroreflex activation therapy, but these treatments have not been tested in dialysis patients.

KG and JKI: Is there any role for diuretics in dialysis patients in terms of BP control or amelioration of heart failure?

Among incident dialysis patients with residual renal function, diuretics can be useful to help remove salt and water in the interdialytic period to minimize the amount needed to be ultrafiltered during dialysis. One observational study suggested the use of diuretics during the first year of hemodialysis to be associated with improved outcomes, however this is likely highly confounded. Among patients on peritoneal dialysis, it is unclear whether or not the use of diuretics affects RRF. Personally, we individualize the use of diuretics. If a patient has good urine output that is enhanced by the use of diuretics without contributing to intradialytic hypotension, then we will continue them. But there is concern about diuretics contributing to hemodynamic instability and faster loss of RRF. Thus, their use needs to be individualized and more studies are needed in this area.

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