Intradialytic Hypotension Strikes Again

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Intradialytic hypotension (IDH) has plagued hemodialysis (HD) patients and their caregivers since the early days of renal replacement therapy. Its persistence in the current era is evident from the results of the 1426-patient Hemodialysis (HEMO) study in this issue of JASN in which a median of 12.5% of dialysis sessions were complicated by IDH requiring saline infusion, lowering the ultrafiltration rate (UFR), or reduced blood flow.1 The last reaction to IDH—reducing the blood flow—is a legacy of the old days of dialysis therapy, when such a reduction might have lessened the vasodilatory effect of acetate influx as well as reduce dialyzer blood volume. It is no longer a helpful intervention.

Patients and nephrologists are all too familiar with the impact of IDH. Patients fear it because of the associated gastrointestinal, muscular, and neurologic symptoms. Nephrologists have long recognized that the organ hypoperfusion resulting from IDH can cause cardiac (infarction, arrhythmias), neurologic (stroke, seizures), or gastrointestinal (mesenteric ischemia) complications.2 More recently, longer term effects of IDH have been recognized, such as an accelerated decline in residual renal function.3 Of particular importance, however, have been the observations of McIntyre,4 who found that IDH results in repetitive, generally asymptomatic cardiac ischemia, resulting in cardiac stunning with, ultimately, irreversible damage to the heart.

To add to the growing list of its adverse consequences, IDH now seems to increase the risk for vascular access thrombosis (VAT), as detailed in a report in this issue of JASN from the HEMO investigators.1 They also found that higher predialysis BP modestly decreases the rate of VAT: A systolic BP 1 SD above the mean was associated with a relative risk for VAT of 0.89. This finding is consistent with previous observations as well as with our understanding of hemodynamics of arteriovenous (AV) access.

The relationship of IDH and VAT is another matter. IDH clearly increases the risk for VAT in patients who undergo dialysis through a central vein catheter while having an unused (maturing) AV fistula (AVF). Here, the hypoperfusion accompanying the IDH places the AVF at risk. However, when the AVF is being used for dialysis, it is not obvious how IDH increases the likelihood of VAT because the blood pump maintains AVF flow irrespective of systemic BP. Considering that the observed association was adjusted for predialysis BP, the basis for the relationship of IDH to VAT is not obvious.

First, is this observation unique? The authors write that it is and that they show, “for the first time, that IDH is significantly associated with AVF thrombosis.” In medical school, I was taught never to say never or always. One might add for the first time to that admonition. In a 2002 report, Puskar et al.5 followed 597 AVF patients prospectively for 5 years and found that both IDH and the lowest diastolic BP during HD both were risk factors for fistula survival. Nevertheless, the study by Chang et al.1 is far more carefully done and closely analyzed, allowing more confidence in its conclusions.

Unlike the weak relationship between predialysis BP and VAT, the relationship between IDH and VAT is far more robust: AVF patients in the highest quartile for IDH were twofold more likely to have VAT than those in the lowest quartile. Oddly, this finding did not apply to patients with AV grafts (relative risk 1.11; NS), despite their much higher underlying thrombotic tendency. It should be noted that these conclusions are based on a somewhat awkward construct necessitated by the available data; data were collected for one treatment per month for each patient, aggregated in 4- to 8-month blocks, and then correlated with the rates of VAT in the subsequent time blocks.

Why does IDH increase the risk for VAT? Given that access flow is maintained during IDH, the explanation must be something other than low-flow–related thrombosis. Perhaps it is the long recognized and frequent autonomic dysfunction seen in patients with IDH that relates it to VAT.6 Such patients are much more likely to have labile interdialytic BP including orthostatic hypotension that might favor VAT.

Another possibility whereby IDH and VAT may be related is through inflammation. High levels of predialysis inflammatory markers (C-reactive protein, IL-6) correlate with unstable intradialytic BP.7 One potentially important source for this inflammation involves the gut: Enteral hypoperfusion such as occurs with IDH may increase intestinal permeability to inflammatory stimuli such as endotoxin.8 When these observations are combined with the finding that inflammatory markers are higher in patients with vascular access dysfunction and correlate positively with neointimal hyperplasia,9...
one may reasonably conclude that systemic inflammation predisposes to both IDH and VAT.

Should these findings influence our clinical practice? The goal of normalizing interdialytic BP will not be altered by the evidence presented. However, normalizing interdialytic BP results in an increased frequency of IDH, a more consequential event for vascular access survival, according to this study, as well as for organ systems whose damage may affect survival.10

Indeed, one may speculate that the difficulties in showing adverse effects from interdialytic hypertension, one of the so-called reverse epidemiology findings seen in dialysis patients, may stem in part from better intradialytic hemodynamics.11

It seems clear that reducing the frequency of IDH is a highly desirable goal on multiple accounts. Its persistence stems from a basic problem: The rate of ultrafiltration required in standard thrice-weekly HD to remove typical interdialytic fluid accumulation and achieve euvolemia often substantially exceeds the rate at which fluid can move from the interstitial to the intravascular space. A number of factors, of course, influence this simplistic analysis (dialysate composition and temperature, patient characteristics), but it remains the underlying reason that, after decades of study, IDH remains so common.

Sticking to this analytic model, it follows that IDH can be reduced by increasing treatment time, decreasing dietary sodium, and increasing interstitial fluid volume by raising dry weight. The beneficial effect of increased treatment time on IDH is more than might be anticipated because of the logarithmic relationship between UFR and IDH: A small increase in time yields a proportionately greater decrease in IDH.12 In addition, the reduction in UFR by itself may reduce mortality risk.13

We write decreasing dietary sodium rather than focus on interdialytic fluid intake to emphasize two points. First, dietary sodium drives fluid intake and weight gain in most patients. Ignoring fluid restriction and concentrating on sodium intake more effectively reduces weight gain than does restricting both—illogical, but perhaps patients just give up from all their dietary restrictions.14 The second reason for emphasizing dietary sodium is that weight gain as a result of primary fluid intake, recognized by predialysis hyponatremia, is far easier to remove without IDH than a similar isonatric fluid load because diffusive sodium gain supports extracellular volume.15

Finally, increasing dry weight is really the default action taken to treat IDH. We may not order it, but patients override us with their low BP. The increased weight expands interstitial volume; the larger this space is, the faster it can be mobilized to replace ultrafiltration-induced declines in plasma volume.16,17

Unfortunately, volume expansion is undesirable and adversely affects mortality.18

The list of adverse consequences from IDH keeps growing. VAT is but one more reason to be concerned about what IDH does to our patients. We can dance around the edges of the problem but it is going to take a change in our traditional thrice-weekly HD regimen to fix it.

DISCLOSURES
None.

REFERENCES


