The study by Shimizu et al1 in this issue of the American Journal of Kidney Diseases concludes that the treatment of intradialytic hypotension with low-volume hypertonic saline and glucose infusions (20 mL each) appears to increase blood pressure by an increase in plasma osmolality and a subsequent rise in the plasma arginine vasopressin (AVP) concentration. This conclusion is supported by the fact that a larger-volume isotonic saline infusion (200 mL) was required to cause a detectable increase in the estimated plasma volume; plasma AVP levels were not altered by the isotonic infusion. Finally, 20-min infusions of both low- and high-dose AVP infusions (2 mU/mL and 4 mU/mL, respectively) raised blood pressure to a comparable degree in patients with intradialytic hypotension. If these conclusions are valid, they point out a previously unappreciated mechanism whereby low-volume hypertonic saline counters intradialytic hypotension, namely via an increase in the AVP concentration and not via an increase in plasma volume.

How important is the problem of intradialytic hypotension and how firm are the conclusions drawn from these new data? First, it is clear that intradialytic hypotension remains one of the most common and vexing adverse effects of standard thrice-weekly hemodialysis.2 It occurs in 20% to 30% of dialysis sessions, and the causes are multifactorial, including autonomic dysfunction, a decrease in plasma volume exacerbated by poor refilling of the vascular compartment from the interstitial compartment, a failure to increase cardiac performance, and peripheral vasodilation,2 to name a few. Similarly, the remedies for the disorder are several and include cooler dialysate temperature, higher dialysate sodium concentration (with and without sodium modeling), a liberalization of “dry weight,” more accurate assessments of “dry weight” by using bioimpedance,3 oral midodrine therapy, and vasopressin infusions, among others.2 One of the major attributes of short daily hemodialysis, nocturnal hemodialysis, and hemofiltration/hemodiafiltration is that these procedures are associated with improved hemodynamic stability when compared to thrice-weekly 3- to 4-hour hemodialysis. Over many years there has been a major effort to decrease the frequency of intradialytic hypotension that has been motivated by the disabling symptoms associated with the condition, the fact that intradialytic hypotension is associated with a higher mortality rate,4 and the inevitable reduction in the dialysis prescription when intradialytic hypotension occurs. Obviously, any enlightenment in the understanding or treatment of intradialytic hypotension would represent a major advance in dialytic care.

The report by Shimizu et al is interesting in this regard. It is important to first note that the protocol was not a crossover design, but instead enrolled several distinct groups of intradialytic hypotension–prone patients. Such a design makes firm conclusions more difficult because, with patients not acting as their own controls, the problem of heterogeneity among dialysis patients makes comparisons problematic and conclusions more tenuous. In addition, as the authors acknowledge, the measurements employed in this study (changes in hematocrit after infusion) are crude estimates of a change in plasma volume. Further, the patients in the study groups were not matched for sex or cause of kidney disease, and this renders the interpretation of the changes in plasma AVP concentrations more problematic. Lastly, the absolute changes in AVP concentrations post–hypertonic saline and glucose were not large and the correlations between AVP levels and blood pressure were not linked in a precise manner.

Despite these limitations, the paper does make several observations of interest. First, it is plausible that a sharp rise in plasma osmolality with low-volume hypertonic saline or glucose could increase blood pressure by mechanisms independent, in part, of an increase in plasma volume. The observed increase in blood pressure is rapid.
and could either be due to a direct effect of the change in the plasma osmolality on resistance vessels, the rise in AVP levels, or both. In the context of these simultaneous changes, the small increase in the plasma volume may also be contributory to the increase in blood pressure. Further, it is of interest that small doses of AVP were highly effective in rapidly improving blood pressure, although this observation has previously been made. Of interest, in the recent paper by van der Zee et al, AVP administration resulted not only in vasoconstriction but also facilitated fluid removal during dialysis. Suffice it to say, just as the etiology of intradialytic hypotension is multifactorial, the mechanisms by which simple remedies for the disorder restore blood pressure are also multiple as interactions between plasma osmolality, the concentration of AVP, and the plasma volume are complicated and incompletely understood. It is likely that an increase in all 3 of these factors is important in restoring blood pressure.

What is badly needed in this area of clinical research are improved methods to reduce the frequency of intradialytic hypotension, thereby avoiding its untoward effects. In this regard, bioimpedance monitors and additional instrumentation to track decrements in plasma volume in real time have proved useful in some settings. Until progress is made in mitigating the incidence of intradialytic hypotension, standard thrice-weekly 3- to 4-hour hemodialysis will continue to be episodically unpleasant.

ACKNOWLEDGEMENTS

Support: None.
Financial Disclosure: None.

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