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Significance of Interdialytic Weight Gain versus Chronic Volume Overload: Consensus Opinion

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Commentary

By Professor Richard Glassock

In late 2012, a group of 18 international experts developed a 'consensus opinion' statement on the significance of interdialytic weight gain (IDWG) versus chronic volume overload, largely involving patients treated with regular (thrice weekly) hemodialysis (HD). This focus is very timely as appropriate evaluation, monitoring and control of extra-cellular fluid volume (ECFV) overload is quickly becoming the most crucial aspect of the modern management of dialysis patients. Indeed, once an adequate Kt/V urea dosing schedule has been attained, ECFV control becomes the clinically dominant issue in patients on intermittent HD treatment for ESRD. This consensus opinion piece contains many great 'pearls' of knowledge and experience-based wisdom and should be read in the original by all dialysis treatment providers, in my opinion.

Very clearly ECFV status on intermittent HD therapy has two distinct components; namely, (i) ECFV that exists at the end of a dialysis session and (ii) the gain in ECFV during the interdialytic interval (assessed as IDWG). As such pre-dialysis ECFV equals the post-dialysis ECFV + the IDWG. The time average ECFV equals the average of the post-and pre-dialysis ECFV and the degree of ECFV volume overload determined by a comparison of estimated values to normal values for the patient's size. Using these criteria a substantial fraction (about 30%) of HD patients have significant chronic ECFV overload (>2.5 l) and much of this continues to exist immediately post-dialysis and is subsequently aggravated by IDWG. Naturally IDWG and ECFV are greatest during the longest inter-dialytic interval. There is little doubt that a higher IDWG (particularly above 3.5–4 kg) is associated with higher mortality and that sodium intake rather than water intake is the primary driver of IDWG. However, IDWG and chronic ECFV overload are governed by different patho-physiological aberrations. IDWG is less in ECFV overloaded patients, and those who achieve subnormal ECFW at the end of dialysis have higher IDWG. Ascribing high IDWG to non-compliance is clearly incorrect. Lower IDWG is often seen in patients with greater residual renal function, and this may be part of the reason for the improved survival of such patients.

Disentangling the independent deleterious effects of excessive intra-dialytic ultrafiltration rates (UFR >10–12 ml/hour/kg BW) needed to return the ECFV to its previous post-dialysis (but expanded) state and the harmful effects of aggravated ECFV overload during the inter-dialytic interval, due to excessive IDWG, can be challenging (see also Flythe JE et al.; Clin J Am Soc Nephrol 2013;8:1151–1161 and the accompanying Editorial Comment by Arora N and Chertow G.; Clin J Am Soc Nephrol 2013; 8:1066–1067). Very clearly short-dialysis treatment sessions, requiring high UFR to accommodate the high IDWG, play a role in the associations with adverse outcomes.

As clearly enunciated by the authors the lack of a universally applied 'gold-standard' method for quantitation of the time-

averaged ECFV overload in HD patients has been a great obstacle to progress. The time-honored but insensitive and inaccurate clinical method of 'dry weight' assessment of ECFV is now largely obsolete and is gradually being replaced by better, more reliable and validated tools, including segmental and whole body multi-frequency bio-impedance spectroscopy (BIS) – with the latter gaining credibility as the most sensitive and accurate way of evaluating and monitoring the status of the ECFV in intermittent HD (and PD as well). Chest ultrasound, evaluating lung water content by the presence of hyperechoic 'rockets', may also be a useful bedside tool. Relative plasma volume (RPV) monitoring (Crit-Line®) techniques can assess overall ECFV status (non-quantitatively) during HD - flat slopes of RPV during ultrafiltration imply ECFV overload, while steep slopes suggest euvolemia. Excess ECFV, assessed y either by BIS, lung-rockets or RPV are associated with excess mortality, left ventricle hypertrophy (often independent of blood pressure) and cardiac dysfunction. Pre-dialysis systolic blood pressure is highly positively correlated with pre-dialysis ECFV expansion and most patients (>80%) can discontinue all anti-hypertensive drugs if time-averaged near euvolemia can be achieved with the proper balance of slow ultrafiltration (sometimes requiring longer dialysis session duration) and rigorous restriction of Na^+ intake during the inter-dialytic interval.

The authors also address the contentious and as yet unresolved issue of the optimal dialysate Na^+ concentration. High pre-dialysis plasma Na^+ concentration is associated with a *higher,* not *lower,* ECFV overload (2.9% excess ECFV per 10 mEq elevation of plasma Na^+ concentration, whereas a low pre-dialysis plasma Na^+ concentration is associated with a higher, not lower, IDWG (0.5% of BW IDWG for each 10 mEq lowering of the plasma Na^+ concentration). At a fixed dialysate Na concentration the dialysate-plasma Na^+ gradient-driven flux of Na^+ (contributing to changes in ECFV status) during dialysis will largely depend on the pre-dialysis Na^+ concentration. A high dialysate to pre-dialysis plasma Na^+ concentration modestly augments IDWG (0.17% of post-dialysis BW per 2 mEq higher dialysate Na^+), regardless of the pre-dialysis plasma Na^+ concentration, but paradoxically a higher dialysate to plasma Na^+ gradient does not apparently deleteriously affect mortality, demonstrating the independent deleterious effects of IDWG.

Conclusion

Many important questions remain in the complex arena of ECFV control in intermittent HD, and their resolution will require carefully controlled prospective trials. Clearly control of ECFV excess should be a primary goal of dialysis treatment, and this assumes dominance over uremic toxin removal once an adequate Kt/V is achieved. Slow ultrafiltration (often requiring longer dialysis session duration) combined with rigorous restriction of intra-dialytic and inter-dialytic Na^+ intake (from all sources including sodium modeling) is paramount. IDWG appears to be of lesser importance, especially if it is being driven by post-dialysis ECFV depletion, but this will require a prospective study to confirm. Prospective trials examining the more recently developed ECFV measurement tools (BIS, RPV, chest ultrasound) on hard-end-points of mortality and hospitalization are needed and some are already in progress. If validated, these tools will supplant IDWG as a surrogate measure of clinically significant ECFV overload. Prospective trials of differing dialysate Na^+ (and dialysate - plasma Na^+ gradients) will help to settle the controversy about selection of the most appropriate standard dialysate Na^+ concentration for intermittent HD. For the time being, a value of around 136 mEq/l for the dialysate Na^+ concentration seems to be a wise choice.

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