Port J Nephrol Hypert 2017; 31(1): 5-6 • Advance Access publication 3 February 2017

Salt and water retention in CKD patients: Too much of a good thing?

Pedro Ponce

NephroCare Portugal

Received for publication: Dec 24, 2016
Accepted in revised form: Feb 1, 2017

A 54-year-old patient with chronic kidney disease (CKD), stage 4, was admitted to the nephrology clinic, in the middle of August: he felt tired; his blood pressure was a little lower than usual; he had no oedema, his haemoglobin level had remained stable for a 6-month period but his serum creatinine had increased from 2.3 mg/dl since the last visit, 6 months ago, to 3.1 mg/dl.

Our main job in the regular follow-up of a CKD patient is to detect unexpectedly rapid progression of renal failure; identify a cause or risk factor for that occurrence and try to reverse it. Dehydration, hypovolaemia and hypotension causing renal hypoperfusion and acute on chronic renal failure are probably the most common culprits for further kidney injury. You stop diuretics, relax salt restriction a little and ask him to increase water intake, right? Well, not always.

Clinical assessment of the hydration status is not an easy task and quite often experts disagree, reaching diverse conclusions. In our physical examination we usually assess intravascular pressure (blood pressure, jugular ingurgitation) and extracellular volume status (oedema), using those parameters to predict intravascular volume and organ perfusion. An audacious leap of faith.

Most of us still have this built-in tendency to allow a certain degree of overhydration, hoping that it will increase renal perfusion and prevent or accelerate recovery of acute kidney injury (AKI) or CKD. Clinical dogma has long dictated that fluid therapy is the treatment of choice for correction of haemodynamic compromise, maintaining adequate renal perfusion and ensuring urine output in patients at risk for renal function deterioration. This dogma is now challenged by robust evidence that fluid overload is associated with AKI, worsening of organ dysfunction and excess mortality[1].

Also, in less dramatic scenarios, there is accumulating evidence of an association of fluid overload with chronic renal failure progression, as well as cardiovascular and all-cause mortality[2].

Endothelial dysfunction appears to be the underlying nephrotoxic effect of fluid overload, through alterations and breakdown of the endothelial glycocalyx, causing capillary leak and interstitial oedema. Fluid overload and interstitial oedema impair renal perfusion by increasing renal venous pressure, ultimately decreasing glomerular ultrafiltration gradient. It is the elevation of central venous pressure that best predicts a decrease in glomerular filtration rate (GFR) and not, as it is usually assumed, a drop in cardiac output[3].

On the other hand, fatigue and decreased muscle strength are among the most common symptoms and complaints of our CKD patients as their disease progresses. They represent a major impairment of their quality of life and a predictor for all-cause mortality[4].

The cause of these symptoms is multifactorial, but the so-called malnutrition-inflammation complex syndrome (MIC) occupies centre-stage in close association with inadequate protein and caloric intake, metabolic acidosis inducing protein catabolism through the ubiquitin-proteasome pathway, enhanced inflammation of the uraemic state, insulin resistance and vitamin D deficiency that contributes to proximal myopathy.

Sodium and intravascular volume balance are usually maintained via homeostatic mechanisms until the GFR falls below 10 to 15 ml/min/1.73m^2. Patients with mild to moderate CKD, despite being in relative volume balance, are less able to respond to rapid intake of sodium and are therefore prone to fluid overload.

In line with concerns over positive fluid balance, some investigators have claimed that limiting sodium intake may help decrease progression of CKD by lowering intraglomerular pressure[5], and the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) organization guidelines recommend that in all adults with CKD, sodium intake should be restricted to <2 g/day unless contraindicated[6].

Exciting new findings allow us now to lump together these two pathogenic pathways, as there is mounting evidence that the malnutrition-inflammation complex and its consequences are apparently closely correlated with fluid overload, although whether MIC is a cause or consequence of fluid overload remains to be clarified[7].

These considerations have led to some comments on a recent paper by Hsiao and co-workers[8]. The authors conducted a cross-sectional study of 172 patients in CKD stages 1 to 5, in one Taiwan hospital. Their goal was to elucidate the effect of body composition (fluid status, lean tissue index [LTI] and fat tissue index [FTI]) on physical function / muscle endurance assessed by handgrip (for the upper extremities), the 30 second chair-stand test (for lower extremities) and the 2-minute step test (for cardiorespiratory endurance) in pre-dialysis CKD patients. They noted, as expected, that CKD patients stage 3 to 5 had higher extracellular water (ECW) to total body water (TBW) ratio than CKD stages 1-2, but there were no significance differences of LTI or FTI among different stages.

Body composition was measured by bioimpedance spectroscopy, using the Fresenius Body Composition Module® (BCM), and physical function was measured only once at enrolment. They found a weak negative correlation between ECW and handgrip strength (r= -0.39) and, somewhat unexpectedly, a negative effect of a higher FTI on muscle strength and endurance.

This study is only a recent addition to an extensive literature on the adverse effects of fluid overload. Not a robust one, though. Cross-sectional in design, small sample, single institution, no prospective longitudinal trend analysis, patients were not stratified according to their CKD stage, introducing a substantial number of confounders. Are muscle weakness and fatigue just consequences of more advanced CKD, which at the same time predicts larger volume overload, or are they indeed interrelated?

Even if the weak negative correlation between excessive extracellular volume and muscle activity is correct, we don´t know if early intervention on fluid retention would preserve physical function.

The BCM methodology is well validated and in my experience a powerful tool to guide our decisions in fluid management; however most studies assessing the side effects of excessive volume and almost all the experience with this device was generated in dialysis patients[9], and its results interpretation have some pitfalls. The machine cannot differentiate intravascular ECW from that in the interstitial compartment, in the context of progressive tissue overhydration seen in muscle-wasted patients with multiple comorbidities[10], and even when BCM recommendation is accurate for the ideal extracellular volume, clinically we may not always be able to reach that fluid status. Cardiovascular impairment and subsequent morbidity caused by end-organs hypoperfusion may occur if we try to decrease volume status as low as recommended, even if rightly so[11].

In summary, we must look at salt and water retention with subsequent hypervolaemia not as the best friend of our patients´ kidneys, but as another example that too much of a good thing can certainly become deleterious.

Disclosure of potential conflicts of interest: The author is an employee of Fresenius Medical Care

References

1. Bouchard J, Soroko S, Chertow G, et al. Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury. Kidney Intern 2009; 76:422-427
2. Tsai Y, Tsai J, Chen S, et al. Association of fluid overload with kidney disease progression in advanced CKD: a prospective cohort study. Am J Kidney Dis 2014;63:68-75
3. Prowle J, Kirwan C, Bellomo R. Fluid management for the prevention and attenuation of acute kidney injury. Nat Rev Nephrol 2014;10:37-47
4. Roshanravan B, Cohen C, Patel K, et al. Association between physical performance and all-cause mortality in CKD. J Am Soc Nephrol 2013;24:822-830
5. Weir M, Fink J. Salt intake and progression of chronic kidney disease: an overlooked modifiable exposure? A commentary. Am J Kidney Dis 2005;45:176-188
6. KDIGO 2012 Clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl 2013;3:5-14
7. Martinez M, Ramirez L, Munoz R, et al. Inflammation in patients on peritoneal dialysis is associated with increased extra-cellular fluid volume. Arch Med Res 2004;35:220-224
8. Hsiao S-M, Tsai Y-C, Chen H-M, et al. Association of fluid status and body composition with physical function in patients with chronic kidney disease. PLoS ONE 2016;11:e0165400
9. Covic A, Onofriescu M. Time to improve fluid management in hemodialysis: Should we abandon clinical assessment and routinely use bioimpedance? Clin J Am Soc Nephrol 2013; 8:1474-1475
10. Chan C, McIntyre C, Smith D, et al. Combining near-subject absolute and relative measures of longitudinal hydration in hemodialysis. Clin J Am Soc Nephrol 2009;4:1791-1798
11. Ponce P, Pham J, Gligoric-Fuerer O, et al. Fluid management in hemodialysis patients. Port J Nephrol Hypert 2014;28:239-248

Correspondence to:
Pedro Ponce, MD
NephroCare Portugal
E-mail: pedro.ponce@fmc-ag.com