Assessment of dry weight in haemodialysis patients by the volume markers ANP and cGMP

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Clinical relevance of the concept of dry weight

The concept of dry weight of a dialysis patient is generally accepted and usually defined as the body weight less than which a normalbuminaemic patient maintained on haemodialysis will become hypotensive with fluid removal, and above which the same patient will be hypertensive and show subtle signs of fluid expansion. This concept is crucial to control hypertension adequately and to avoid risks of intradialytic hypotension. The exact determination of post-dialysis dry weight by clinical acumen is an exercise that often taxes the clinical judgement of even the most astute nephrologist. In certain diseased states associated with end-stage renal failure, clinical evaluation is unreliable in assessing dry weight. In fact, 25–50% of patients on chronic haemodialysis have an incorrectly determined dry weight [1,2]. The morbidity of dialysis therapy may be increased in each instance. With the increased number of both elderly multimorbid patients and patients with primary heart disease entering the chronic dialysis programme, exact estimation of dry weight seems to be of even more clinical importance.

We have questioned, in a series of clinical studies, whether the volume status of stable patients undergoing regular maintenance dialysis could be assessed more objectively using the pre-dialysis or post-dialysis plasma atrial natriuretic peptide (ANP) or cyclic 3',5'-guanosine monophosphate (cGMP) concentrations.

Plasma ANP and cGMP in patients on dialysis

ANP and its second messenger cGMP are elevated in patients with end-stage renal disease requiring treatment either with the artificial kidney [3–6] or continuous ambulatory peritoneal dialysis (CAPD) [7]. Elevated plasma concentrations of these markers in end-stage renal disease are attributed, predominantly, to an enhanced release of ANP in response to an increased wall stress in the atra of the heart and, in part, to a reduced clearance of the substances [8]. Excessive plasma concentrations of ANP or cGMP have been found immediately prior to dialysis in uraemic patients with co-existent congestive heart failure or valvular heart disease [5,9]. Plasma ANP and cGMP were found to be reduced after haemodialysis or haemofiltration, but usually remained greater than the normal range despite fluid volume reduction to normal or even less [3,6]. This implies that factors other than simple volume overload can contribute to elevation or reduction of these markers in dialysis patients. These factors may include reduced clearance by the mode of renal replacement therapy, clinically
unsuspected cardiac dysfunction or rapid shifts between intravascular and extravascular compartments [10]. Compared to haemodialysis, patients on continuous ambulatory peritoneal dialysis showed plasma concentrations of cGMP and ANP less than the pre-dialytic and post-dialytic values of haemodialysis patients [7].

Plasma ANP and cGMP as markers for dry weight in haemodialysis patients

Measurements of pre- and post-dialysis plasma ANP and cGMP in an unselected population of 81 patients on regular haemodialysis demonstrated that a post-dialytic plasma cGMP less than 20 pmol/ml correctly assessed the patients dry body weight (Figures 2 and 3) [5]. None of these patients had clinical, radiological, echocardiographic or sonographic evidence of fluid overload. Post-dialytic plasma cGMP and change in body weight correlated close enough to be suitable for clinical use \( r = 0.85 \) compared to pre-dialysis cGMP values or ANP levels [3].

Validation of post-dialysis cGMP with other non-invasive techniques for assessment of dry weight

Pre- and post-dialysis ANP concentrations have been successfully validated against the right atrial [11,12] or pulmonary wedge pressure [12], which may be considered the gold standard for the estimation of fluid status. Excluding patients with dilated left atrium, the relation between cGMP and the vena cava diameter was found to be highly significant [13]. There was also a positive correlation between vena cava diameter and delta cGMP in these patients [13]. While electrical conductivity measurements in dialysis patients were not significantly related to pre-dialysis ANP and cGMP, post-dialysis cGMP but not ANP concentrations showed a significant correlation [2].

Determination of post-dialytic cGMP in dialysis patients: indications and limitations

Determination of cGMP after haemodialysis should be performed in adults and in children, for individual attainment of dry weight after initiation of dialysis therapy or after severe intercurrent diseases, or for follow-up evaluation of hypertension or heart disease. This simple non-invasive method may also be of value in dosing diuretics and antihypertensive drugs in advanced renal failure or for documentation of intravascular volume state in association with scientific investigations.

However, in patients with chronically altered left or right atrial haemodynamics, both ANP and cGMP are difficult to interpret. Plasma concentrations of these markers are not able to distinguish hypovolaemia from normovolaemia.

Conclusion

There is no gold standard for the assessment of dry weight in patients with end-stage renal disease receiving non-transplant renal replacement therapy. All methods implicated have limitations either by patients' characteristics or by general clinical practice. Clinical evaluation of the patients' state remains the first step, but should be supplemented by the regular post-dialytic determination of plasma cGMP for long-term monitoring of the intravascular fluid volume state. Technical investigations should follow if the patient becomes instable according to clinical and biochemical data.
Fig. 3. Plasma cGMP after dialysis in 81 chronic haemodialysis patients (left) and in 21 of these patients after reduction of dry body weight (right). Patients with radiological signs of pulmonary congestion are marked as squares. All seven patients whose cGMP remained greater than 20 pmol/ml despite reduction of body weight had documented heart disease with left ventricular dysfunction.

References