Dialysis schedule-related fluid state and cardiovascular effects

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Introduction

The oscillation of the fluid state in anuric patients is dependent on the type of dialysis, which has to mimic excretory renal function. Typically, in haemodialysis (HD), patients’ fluid state is in a continuous disequilibrium characterized by a rapid reduction during dialysis and a slow increase between dialysis sessions. Maxima and minima of the cyclic fluctuations of body water (and sodium) are determined by the physician’s prescription (target weight) and by the drinking and eating habits of the patients (pre-dialysis weight). Both extremes of fluid state have to be compensated by the cardiovascular system of dialysis patients, which frequently is in an abnormal state. Typical cardiovascular complications can occur originating from all three determinants: dialysis target weight can be erroneous and the mode of the dialysis technique can be inadequate; the fluid intake of the patients may overwork the cardiovascular compensation capacity; and, finally, a pathological cardiovascular system responds differently to the stress of fluid fluctuation.

Fluid-dependent signs and symptoms

In chronic dialysis patients without acute disease, some signs and symptoms occur at distinct phases of the fluid cycle. However, all signs and symptoms can have a multi-factorial origin, and only in the case of regression after fluid correction do they appear to be specifically volume related. In the pre-dialysis phase, a patient frequently is hyperhydrated, which can translate into sudden dyspnoea during exercise, while recumbent or while sitting, and this can culminate in pulmonary oedema. Ankle or tibial oedema can be present. Hypervolaemia is not the only cause of arterial hypertension in dialysis patients, albeit that it is the most important and most frequent. It has been shown that salt loading increases the arterial pressure of patients with renal failure in contrast to healthy persons [1], and that systolic blood pressure is significantly increased during hypervolaemic periods in HD patients [2]. Furthermore, a paradoxical increase in blood pressure during ultrafiltration in HD patients can occur in the presence of overhydration [3]. Overhydration can lead to a wide spectrum of cardiac changes depending on the pre-existing cardiac state: hypercirculation, characterized by an increased cardiac output, can be one sequela. Another reaction pattern can be cardiac dilatation, characterized by increases in the diameters of the vena cava, right atrium, left atrium and right and left ventricles [4].

In some patients with end-stage renal failure, cardiac enlargement associated with a reduced left ventricle (LV) function can be present without other evidence of hyperhydration. Initiation of dialysis and water removal to normovolaemia can regress cardiac dilatation and restore normal cardiac function.

Symptoms of hypovolaemia most frequently occur during or immediately post-haemodialysis and ultrafiltration. Although plasma volume is an integral part of the extracellular volume and the equilibrium between the two compartments establishes eventually, refilling of plasma volume takes some time and clearly depends on the degree of overhydration [5,6]. Primarily with high ultrafiltration rates, as necessitated in short dialysis sessions, vascular underfilling can lead to ventricular underfilling and eventually to dialysis hypotension [7]. Thus, dialysis hypotension need not necessarily be a consequence of hypovolaemia and an incorrectly defined dialysis target weight. The same is true for symptoms such as muscle cramps. On the other hand, suddenly occurring fatigue, low blood pressure, cramps and hypotension can be taken as hypovolaemic signs when the dialysis schedule has not been altered and has been tolerated without symptoms during preceding sessions.

The incidence of dysvolaemic periods in dialysis patients is virtually unknown. By clinical standards, only about half of the patients are in a state of normohydration, about one-third are hypovolaemic and a quarter are hypervolaemic (Table 1). Whether dysvolaemia is an independent risk factor in the prognosis of dialysis patients still awaits further elucidation. There are three lines of indirect evidence that this may well be the case: Kramer et al. published data from the (at that time still incomplete) EDTA registry of increased mortality in dialysis patients with excess...
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Table 1. Proportion of dysvolaemic periods

<table>
<thead>
<tr>
<th>Percentage of dysvolaemic periods (n = 157)</th>
<th>Fluid correction necessary to restore normovolaemia (target weight change)</th>
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</thead>
<tbody>
<tr>
<td>Hypovolaemia 35%</td>
<td>940 ± 584 g</td>
</tr>
<tr>
<td>Hypervolaemia 20%</td>
<td>2409 ± 2230 g</td>
</tr>
<tr>
<td>Normovolaemia 45%</td>
<td>–</td>
</tr>
</tbody>
</table>

weight gain between dialyses [8]. In the same report, an increased rate of cardiac death in German male patients on short duration dialysis was published. Secondly, diabetic patients on dialysis, who had an increased incidence of dialysis hypotension, simultaneously had a worsened cardiac prognosis [9]. Thirdly, Tassin reported outstanding survival data based on the absence of arterial hypertension, achieved by low ultrafiltration rates and (in comparison with other centres) minimal weight gains between dialyses [10].

Prevention of acute cardiovascular effects appears difficult to achieve in the common schedules of intermittent short duration HD. Rigid time schedules impede necessary flexibility, where individual ultrafiltration rates within a safety margin should be applied in order to prevent vascular and cardiac underfilling. The problem of frequent dysvolaemia in HD patients appears to be connected with rigid dialysis duration schedules. It might be speculated that the published prevalence of > 70% of arterial hypertension in American dialysis patients may originate from an inappropriate control of hypervolaemia [19]. The dehydration puzzle of prevention of dialysis hypotension and simultaneous prevention of interdialysis hypertension can only be solved by a change in dialysis schedule, such as prolonging sessions or introducing additional sessions, which might attenuate the extremes of the volume cycle. In addition to a regular clinical monitoring of the volume state, methods such as inferior vena cava sonography and bioimpedance are helpful in assessing the volume state [11–13] (Table 2). However, it is safe to say that these methods usually do not allow an acute discrimination of dysvolaemia [2,14] due to a large inter-patient variation; on the other hand, both methods are predictive in a regular follow-up [2]. Data on the volume state of peritoneal dialysis patients are sparse and rather point towards constant hypervolaemia.

Dysvolaemia and co-existing cardiac disease in dialysis patients

Left ventricular hypertrophy (LVH) and ischaemic heart disease are the two most frequent cardiac entities which render dialysis treatment more difficult. Both cardiac diseases worsen the prognosis in dialysis patients [15,16]. At present, it is unclear which aspect of uremia or dialysis treatment might be associated with an impact on prognosis. On the other hand, pathophysiologically orientated studies clearly point to involvement of the volume state.

It has been shown that LVH frequently is associated with LV diastolic dysfunction [17]. Thus, LV diastolic filling is disturbed, caused by a greater stiffness of the ventricular walls. In relatively young HD patients, mean end-diastolic pressure at rest is about double that of healthy persons, and the relationship between LV volume and LV pressure is abnormally steep [18], indicating a reduced LV compliance. For dialysis patients, this is a very significant finding since both extremes of the volume cycle will be amplified in its cardiac effects. Hypervolaemia and thereby an LV volume load will be accompanied by an inappropriately steep increase in LV pressure frequently reaching thresholds for LV backward failure such as pulmonary congestion and pulmonary oedema. This situation often is present pre-dialysis, when patients are in hypervolaemia, particularly at the end of a long dialysis interval. The opposite situation occurs during rapid ultrafiltration, where the characteristics of the steep volume–pressure relationship cause an inappropriate fall in LV pressure which clinically translates into impaired LV filling and eventually dialysis-associated hypotension or shock. It has been shown that dialysis patients with reduced LV compliance are prone to this complication [18]. Therapeutic consequences lie in a dialysis regimen which prevents hypervolaemia, as well as high ultrafiltration rates. This can be achieved either by long duration sessions or by a more frequent dialysis schedule.

A second frequent cardiac disease co-existing in dialysis patients is ischaemic heart disease, which also

Table 2. Methods for the follow-up of volume state

<table>
<thead>
<tr>
<th>Method</th>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitoring of signs and symptoms</td>
<td>Measures the whole spectrum of dyshydration</td>
<td>Unspecific</td>
</tr>
<tr>
<td>Vena cava sonography</td>
<td>Sensible as follow-up method</td>
<td>Occurring late</td>
</tr>
<tr>
<td>Bioimpedance</td>
<td>Sensible as follow-up method</td>
<td>Measures only parts of the volume cycle</td>
</tr>
<tr>
<td></td>
<td>Estimates ECV</td>
<td>Not applicable with tricuspic incompetence</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Interpretable measurements only 1–2 h post-HD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Measures only parts of the volume cycle</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reproducibility disturbed by food and fluid intake; electrolyte disequilibrium</td>
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</tbody>
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has an impact on prognosis [16]. Myocardial ischaemia can be induced by a narrowing or obliteration of the large epicardial vessels (coronary artery disease), by a reduced number of small intramyocardial vessels or by functional intramyocardial perfusion disorders. The driving pressure for myocardial perfusion during diastole is generated by the gradient between diastolic aortic pressure and ventricular diastolic pressure. In the dialysis patient, there are many conditions which can reduce this perfusion gradient: elevated LV end-diastolic pressure (by reduced compliance associated with LVH or ischaemia) or low diastolic aortic pressure due to reduced aortic compliance. Furthermore, myocardial oxygen demand can be augmented by increased cardiac work, due to tachycardia and high LV systolic pressures necessary for filling a less compliant aorta. The dialysis schedule can interfere in many ways: hypervolaemia increases LV diastolic pressure and can be accompanied by hypercirculation; and intravascular underfilling during HD can reduce diastolic aortic pressure. Consequently, it has been shown that abolishing hyperhydration in dialysis improves myocardial perfusion and that diabetic patients with a suspected high prevalence of cardiac macro- and micro-vessel disease have a worsened prognosis due to dialysis hypotension.

Again, the cornerstones of therapy are prevention of hyperhydration and dialysis-associated hypotension (besides improvement of anaemia and specific drug therapy). Clinical experience shows that in angina pectoris-prone dialysis patients the most severe symptoms occur at the end of the weekend intervals of dialysis and, conversely, that such episodes can be prevented or reduced in severity by an additional dialysis. With respect to the high prevalence of cardiac disease and the potential dangers of volume oscillation, more frequent HD sessions are desirable, at least in patients with proven cardiac disease.

References