Advising dialysis patients to restrict fluid intake without restricting sodium intake is not based on evidence and is a waste of time

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Introduction

Advice on the restriction of fluid intake is a cornerstone of management of patients with kidney failure. Doctors ‘prescribe’ fluid restrictions on ward rounds for patients with acute renal failure. Nurses on the dialysis unit, backed up by dieticians and psychologists, exhort patients to drink less, telling those with large inter-dialytic weight gains that they are putting themselves at risk of heart failure and death. Written information for patients invariably emphasizes the importance of fluid restriction, as do textbooks of renal medicine and dialysis. Here, I argue that much of the effort expended persuading patients to drink less is misdirected.

There is no doubt that fluid intake is the most important determinant of weight gain between one session of haemodialysis and the next, particularly in patients with minimal residual urine output. Small amounts of water can be lost in the form of sweat but these losses generally amount to not much more than 500 ml per day in the cool climate we have in most of
Europe. In patients with normal bowel function, the amount of water lost in the stools is small. However, it is arguable that fluid intake is determined, in turn, by sodium chloride intake.

**Do patients with high inter-dialytic weight gain have a higher risk of death?**

No. The largest study examining this issue showed the reverse: it is those patients with low inter-dialytic weight gain that are at highest risk of dying, although it is true that very high inter-dialytic weight gains were also associated with a modestly increased risk [1]. The most likely explanation for this surprising finding is that low inter-dialytic weight gain is associated with poor nutritional intake, and may be a marker for serious co-morbid disease. This explanation was confirmed by a study showing that low inter-dialytic weight gain was associated with poor nutritional status, itself an important predictor of poor outcome in dialysis patients [2]. In another smaller study, high inter-dialytic weight gain was associated with increased mortality in diabetic, but not in non-diabetic, haemodialysis patients [3]. High inter-dialytic weight gains may contribute to hypertension in dialysis patients [4–7], but most studies show no such relationship [8–13] or only in a subset of ‘volume-responsive’ patients [14]. This lack of a relationship is less surprising than it seems, because it is the change in plasma volume, not in total extracellular volume or total body water, which is likely to result in acute changes in blood pressure during fluid removal [15].

One study has shown that sudden and cardiac death rates amongst haemodialysis patients are higher after the ‘long gap’ (e.g. Mondays for Monday/Wednesday/Friday patients) than on other days of the week [16], but whether this increased mortality is a result of fluid overload or to electrolyte abnormalities such as hyperkalaemia is not known.

**The relationship between water intake and ECF volume depends on sodium intake**

The average 70 kg person contains about 40 l of water. Two-thirds of this is intracellular, and of the one-third that is extracellular, most is interstitial fluid; circulating volume is around 4 l, of which plasma water makes up around 50% (2 l), depending on haematocrit. The distribution of extra water ingested in a dialysis patient depends on the amount of salt–sodium chloride—that is ingested with it. If no salt is ingested, we would expect 1 l of water to be distributed evenly across total body water, two-thirds entering cells and one-third remaining in the extracellular compartment, of which 2/40th of 1 l, 50 ml, would be in plasma water. However, if 140 mmol sodium is ingested with each 1 l of water, simple physiology would predict that all the water will remain in the extracellular space, with a greater increment in circulating volume.

Think what happens to the serum sodium concentration of a typical dialysis patient. In general, it is very unusual to see serum sodium concentrations outside the normal range (either too high or too low), and most dialysis patients have a pre-dialysis serum sodium concentration of around 138 mmol/l. If an anuric patient comes in 4 kg over their target weight, having left the dialysis unit 44 h earlier with a serum sodium (equal to the dialysate sodium concentration) of 138 mmol/l, and has a pre-dialysis sodium concentration which is still 138 mmol/l, this implies that the patient has not only ingested 4 l of water but also $138 \times 4 = 552$ mmol of sodium since their last dialysis. This represents a sodium intake of just over 276 mmol/24 h. A normal human can remain healthy on a sodium intake of 10 mmol/24 h, but the average Western diet contains 10–15 times this much, and the huge amounts of sodium in many processed foods mean that many people in the UK have a dietary sodium intake of well over 200 mmol/24 h.

**Where does the extra fluid accumulate in haemodialysis patients?**

The distribution of fluid between the extracellular and intracellular compartments can be studied using multi-frequency bio-impedance techniques, which rely on the fact that the electrical resistance of cells is different to that of extracellular fluid. One study using this technique showed that fluid gained between dialysis sessions largely remains in the extracellular space [17]. The only possible reason for this is that the extra fluid is held in the extracellular space by extra sodium, ingested during dialyses. Another study using A-mode ultrasound measurements of the tissue thickness over the forehead and tibia showed marked reduction in tissue thickness during fluid removal on dialysis, and the authors calculated that 45% of fluid withdrawn during dialysis is stored in these ‘superficial shell tissues’ [18].

Remember that oedema may not become clinically evident until there is extracellular volume overload of up to 10% body weight [19].

**What governs fluid intake in dialysis patients?**

Patients drink for one of two reasons: thirst, and because they just ‘feel like a drink’—for example, social drinking. It is very difficult indeed for a conscious patient to ignore thirst, and severe thirst will drive a patient to find fluid wherever they can—for example, drinking the water from the flower vase. When patients do this, it is not because they are ‘mad’, ‘totally non-compliant’, or ‘too stupid to understand the importance of fluid restriction’—it is because it is nearly impossible to ignore such a strong
physiological stimulus. The over-riding stimulus to thirst is effective plasma osmolality, of which serum sodium concentration is the major determinant; other contributors are hypovolaemia and angiotensin II. Using hypertonic saline infusions, Argent et al. demonstrated normal osmotic thresholds for thirst and ADH release in patients about to commence dialysis therapy [20]. It follows that no dialysis patient whose sodium intake exceeds sodium output will be able to resist the stimulus to drink to maintain serum osmolality within the normal range, unless first rendered unconscious!

Two things follow from this simple argument.

- We should concentrate on advising and helping dialysis patients to limit their *salt* intake, which will help limit thirst.
- Advising dialysis patients to restrict fluid intake when they have not had advice on how to limit their salt intake is inhumane, because they are being made to feel guilty and inadequate at being unable to restrict their fluid intake—and is a waste of time.

A few patients will remain desperately thirsty despite tight restriction of dietary sodium, as a result of high renin and angiotensin II levels [21,22], and one controlled trial shows that ACE inhibitors can reduce thirst and weight gain in dialysis patients with habitually high inter-dialytic weight gain and fluid overload [23]. However, this may not be the whole story: patients with increased inter-dialytic weight gain have a decreased thirst threshold (measured during hypertonic saline infusion) compared with other haemodialysis patients, but this difference was not attributable to differences in plasma angiotensin II [24].

Hypovolaemia can also stimulate thirst, of course, so inappropriately low target weights might cause thirst as well as increased appetite for salt. This is probably less much common as a cause for thirst than salt overload.

**What is the impact of dialysate sodium?**

Standard dialysate sodium concentration has increased over the past two decades from around 130 to sometimes over 140 mmol/l, because higher dialysate sodium is thought to prevent the cramps and symptomatic hypotension which otherwise frequently complicate dialysis, particularly as the duration of dialysis has been decreased towards 4 h or even lower. However, several studies have shown that reduction of dialysate sodium together with advice to reduce dietary sodium intake can result in marked improvement in blood pressure, and also in inter-dialytic weight gain [25]. Regression of left ventricular hypertrophy has also been reported [26].

One small study in a North American dialysis centre utilizing a dialysate sodium of 142 mmol/l showed that pre-dialysis sodium was constant in individual patients, but varied considerably from patient to patient, probably as a result of differences between individuals in thirst threshold. The gradient between dialysate sodium and pre-dialysis sodium concentration was closely correlated to inter-dialytic weight gain and mean arterial blood pressure. The authors suggested that dialysis should be individualized, with dialysate sodium being set to match the individual patient’s pre-dialysis sodium concentration [27]. Such a policy would reduce unnecessary thirst, weight gain, and hypertension caused by dialysing sodium into patients.

In peritoneal dialysis too, low sodium dialysate results in reduction in blood pressure [28].

Sodium profiling during dialysis has been promoted as a way of improving cardiovascular stability during dialysis without causing net sodium gain. This technique is based on the assumption that extracellular sodium will remain ‘clamped’ at the final dialysate sodium concentration. However, this assumption has never been tested adequately. It is quite possible, for instance, that high extracellular fluid sodium concentration results in flux of water from cells. This results in intracellular dehydration, which might then cause rebound hypernatraemia after completion of dialysis, which might explain why some sodium profiled patients appear to become more thirsty, resulting in a vicious cycle of increasing fluid gains and increasing symptoms during rapid volume removal on dialysis. Recently published evidence supports this, showing a significant decrease in intracellular volume (measured by bio-impedance) and in red cell volume during haemodialysis using a dialysate sodium of 143 mmol/l compared with a dialysate of 138 mmol/l [29].

**How else may sodium overload influence blood pressure?**

One of the intriguing observations in patients undergoing long slow dialysis at Tassin, where blood pressure is nearly universally controlled with salt restriction and fluid removal on dialysis [30], is that compared with patients undergoing standard dialysis, peripheral vascular resistance is low—whereas one might expect a higher peripheral vascular resistance as a result of vasoconstriction in response to relative extracellular volume depletion [31]. The cause of this paradoxical vasodilatation is not certain. It may relate to a more efficient removal during long slow dialysis of vasoconstrictor substances, although these have not been identified. Alternatively, hypertension in patients receiving standard dialysis may relate to increased vascular wall sodium [32], slow removal of which during the first few weeks of long slow dialysis and dietary sodium restriction, causing gradual vasodilatation, would neatly explain the ‘lag phase’ between the reduction of target weight and the subsequent fall in blood pressure [33].
What might the dangers be of ‘allowing’ free fluid intake in dialysis patients?

Water ingested without sodium will distribute throughout total body water, and will, therefore, have much less impact on extracellular volume. The water load would cause a small drop in extracellular sodium concentration. This would result in a greater osmotic gradient between dialysate and plasma during dialysis, favouring rapid removal of the extra water. Theoretically, a high water load could result in hyponatraemia, and the increased cell volume caused by water entering cells could cause cerebral oedema. Some advice to avoid excessive water intake would, therefore, remain necessary. However, if my reasoning is correct, it would be possible to advise patients simply to drink when thirsty and to avoid excessive ‘social’ drinking, and no longer necessary to advise patients to attempt to ignore thirst. One small prospective randomized controlled trial has examined this strategy: 28 haemodialysis patients were randomized to very low sodium intake, with advice to drink only when thirsty, or to standard diet and fluid intake. During the low sodium diet, weight gains were significantly lower, despite free fluid intake, than on the standard diet [34].

Where is the catch?

The drawback to this argument is the practical difficulty of persuading patients to limit dietary sodium intake. The high sodium content of many processed foods means that simply avoiding extra salt at the table and in cooking will not be enough to reproduce the effects of tight dietary sodium intake described in this article. However, any reduction in salt intake is likely to have a beneficial effect in the right direction.

Conclusions

- Look after the salt intake, and the water will look after itself. Even a reduction of sodium intake to 100 mmol/day, which is readily achievable, would make a dramatic difference to thirst and weight gain in many patients.
- Dialysis and processed foods are the main sources of salt excess.
- Low weight gains should cause more alarm than high weight gains.
- Weight gain between dialyses bears little relationship to plasma volume or to blood pressure.
- Most dialysis patients want to stay alive, and will, within reason, do what is asked of them. Asking patients with severe thirst to drink less than 1 l a day is illogical, inhumane, and should become part of the history of dialysis in the twentieth century. Twenty-first-century patients deserve better.

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References

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