Volume Effects of Daily Hemodialysis

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Daily hemodialysis appears to be well tolerated, with hypotension rarely complicating such therapy, a finding that is the subject of this review. When daily hemodialysis utilizes a shorter treatment time, this may limit the intradialytic reduction in plasma volume. This reduction is a function of treatment time, ultrafiltration rate (UFR), and plasma refilling rate (PRR). However, daily therapy may be associated with a higher UFR and lower PRR, both of which may accentuate the fall in plasma volume. The reduced frequency of intradialytic hypotension may, in part, be related to other aspects of such therapy, such as the smaller oscillations and decreased dialytic flux of hemodynamically active solutes.

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Key words

Daily hemodialysis, dialysis-related hypotension, potassium, ultrafiltration rate, plasma volume, plasma refilling rate

Introduction

Considerations of volume impact the dialysis patient in two ways. First, the acute removal of the fluid gained during the interdialytic interval can result in intradialytic hypotension, a frequent complication of chronic hemodialysis (1). The second effect is that arising from a patient's chronic volume status. Dialysis patients are commonly volume-overloaded [as assessed clinically or by newer investigated methods (2–6)], a finding that contributes to hypertension, left ventricular hypertrophy (independent of hypertension), and heart failure (7–9).

Acute changes in a dialysis patient's volume status are reflected in the patient's interdialytic weight gain, intradialytic weight loss, and postdialysis body weight. Nephrologists usually encourage patients to minimize their interdialytic weight gain and seek to reduce the patient's postdialysis (dry) weight to the lowest, clinically tolerated level. Many chronic dialysis patients are maintained at dry weights that are recognized to be higher than those that are considered ideal due to intradialytic hemodynamic problems that occur when such ideal dry weights are sought.

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There are insufficient data on the effect of daily hemodialysis on intradialytic blood pressure and postdialysis (dry) weight to make any definitive conclusions regarding the procedure's impact on these two aspects of volume. Such data as do exist, however, strongly suggest that daily dialysis allows the required fluid removal to be accomplished with little intolerance (hypotension, cramps) as well as allowing for an acute reduction in postdialysis weight (10). The purpose of this article is to consider the reasons for this apparently greater tolerance of fluid removal with daily compared to thrice-weekly hemodialysis.

The single most important factor responsible for the development of intradialytic hypotension is an ultrafiltration-induced fall in plasma volume (11). Fluid removed by ultrafiltration comes directly from the plasma space. The fluid removed is substantially (but not completely) replaced by fluid moving from the interstitial and intracellular spaces to the plasma space. The rate at which this movement occurs is called the plasma refilling rate (PRR). The extent to which the ultrafiltration rate (UFR) exceeds the PRR determines the extent of the intradialytic fall in plasma volume (12).

An appropriate place to start in considering the volume effects of daily hemodialysis is to examine the relative changes in plasma volume during daily 90-min hemodialysis versus thrice-weekly 3.5–4 hour hemodialysis. The most superficial analysis clearly suggests that plasma volume will be better maintained with the shorter treatment, since the size of the reduction in plasma volume is the product of treatment time and the difference between the ultrafiltration rate and the plasma refilling rate (UFR – PRR) (Figure 1). If the UFR and the PRR were the same during both daily hemodialysis and standard hemodialysis, then, by virtue of the shorter treatment time, the extent of the reduction in plasma volume would be lower in daily dialysis. This would easily explain a better tolerance of fluid removal during daily hemodialysis.

What is the UFR during daily hemodialysis?

If weekly fluid intake were similar in patients receiving daily and thrice-weekly hemodialysis, then the UFR during the two procedures would be a sole function of the relative total treatment times. Daily 90-min dialysis provides 10.5 hours of treatment per week, which is equivalent in total treatment time to three 3.5- hour hemodialysis sessions weekly. On the basis of total treatment time, then, UFRs would not be expected to differ substantially between the two procedures.

However, Buoncristiani found that the average UFR during daily hemodialysis in his patients was 1.4 L/hour, a rate

Plasma Volume, Plasma Refilling, and Ultrafiltration During Dialysis

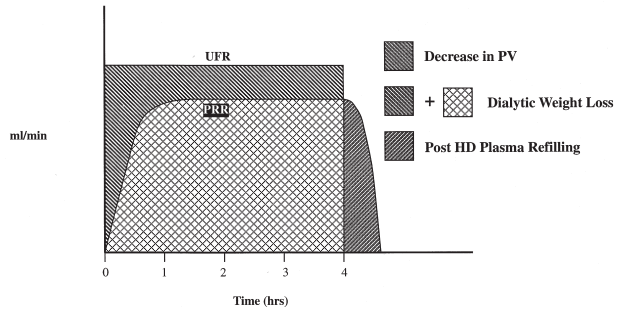

FIGURE 1A A fixed ultrafiltration rate (UFR) over a 4-hour treatment is shown. The plasma refilliing rate (PRR) rises quickly as plasma oncotic pressure increases and vascular hemodynamics change. Plasma refilling continues after the treatment ends. The area between the UFR line and the PRR line represents the intradialytic decrease in plasma volume.

Plasma Volume, Plasma Refilling, and Ultrafiltration During DailyDialysis

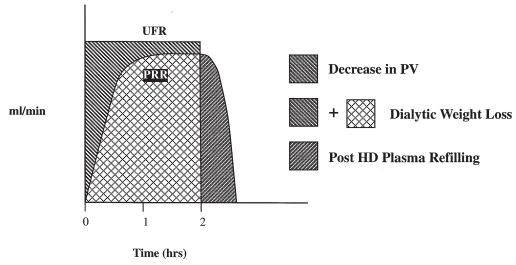

FIGURE 1B With a similar UFR and PRR and a shorter treatment time (2 hours in this example), the intradialytic reduction in plasma volume will be smaller than with a longer treatment time.

substantially in excess of the usual ultrafiltration rate in thrice-weekly hemodialysis (10). The cause of the increase in fluid intake that must have been present in these patients is speculative. It may reflect an improvement in a patient's sense of well-being and, as a consequence, an increased nutritional intake. It may also reflect a loss of "negative" feedback from a reduction in symptomatic intradialytic hypotension (*vide infra*).

What is the PRR during daily hemodialysis?

The extent of the reduction in plasma volume for a given rate of fluid removal varies markedly during hemodialysis among individual patients. Among 21 patients subjected to 2 L of ultrafiltration over 60 min, the fall in plasma volume ranged from about 1% to over 20% (13). By definition, these patients had marked variability in their rate of plasma refilling. A major determinant of this rate is the size of the interstitial fluid (IF) space. Patients with large IF volumes refill their plasma space much more rapidly than those who have a small IF volume. This is consistent with the clinical observation that patients who are markedly above their dry weight (i.e., have a substantial amount of edema) tend to tolerate ultrafiltration much better than those who are at or close to their dry weight. It also explains why increasing a patient's dry weight lowers the frequency of intradialytic hypotension. Thus the degree of volume overload (or volume depletion) in a patient is a major determinant of the PRR.

Two consequences of daily therapy are a shorter time period between treatments and a reduction in the size of the interdialytic oscillation in body weight. These changes will reduce the extent of fluid overload (and IF volume) in the predialysis state and reduce the average PRR during dialysis. Further contributing to this theoretical reduction in PRR is the observation that soon after beginning daily dialysis there is a fall in a patient's dry weight as a result of the improved tolerance to ultrafiltration. In Buoncristiani's study, patients' dry weight fell about 2 kg within a brief period after beginning daily treatment, indicating a further fall in IF volume (10). These two factors should, theoretically, have a significant negative impact on plasma refilling during daily dialysis.

If daily dialysis requires a higher UFR and is accompanied by a lower PRR than thrice-weekly dialysis, it is not necessarily the case that the shorter treatment times with daily therapy will routinely be accompanied by a smaller reduction in plasma volume than thrice-weekly dialysis (Figure 2). Nevertheless, hypotension was rare (approximately 2% of treatments) in Buoncristiani's study (10).

While plasma volume is a major factor determining tolerance to fluid removal during dialysis, it is modulated by many other factors (1). The likelihood of hypotension developing in association with a given reduction in plasma volume depends on the effectiveness of compensatory mechanisms. These mechanisms act via decreases in venous capacity, increases in peripheral vascular resistance, and/or cardiac output (14). The effectiveness of these mechanisms may differ in daily and thrice-weekly hemodialysis.

It is reasonable to assume that the body's response to plasma volume reduction might be influenced by blood levels of various solutes and toxins; thrice-weekly and daily dialysis differ substantially in this regard. In addition to reducing oscillations in volume, the shortened interdialytic period associated with daily dialysis also reduces oscillations in solute levels. Thus the blood levels and dialytic flux of many solutes, some with hemodynamic importance (Table I), will differ between the therapies. One example of such a solute is potassium. With daily therapy the quantity of potassium removed during each treatment is lower, and the postdialysis serum potassium levels are higher (Figure 3). Considerable

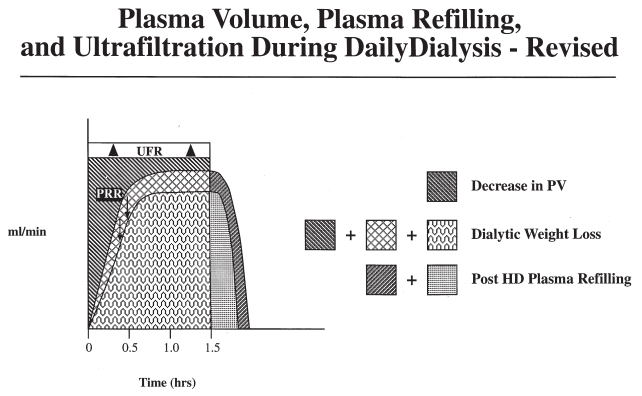

FIGURE 2 Data suggest that the UFR is higher in daily hemodialysis (shown here as a 90-min treatment) than with standard therapy as a result of greater fluid intake. There is also reason to think that a major determinant of PRR, interstitial fluid volume, is reduced in daily therapy. Therefore, the area shown as representing the decrease in plasma volume may be expanded to include the additional area (volume) enclosing the triangles and the arrows. Thus, despite the shorter time, it is not clear whether the intradialytic reduction in plasma volume is reduced with daily therapy.

TABLE I Solutes, toxins and volume: standard versus daily hemodialysis (HD)

	Standard HD	*Daily HD*
Predialysis levels	Higher	Lower
Dialytic flux	Larger	Smaller
Postdialysis levels	Lower	Higher

Consequences for:
Potassium, magnesium, middle molecules, water, osmolality, hydrogen ion, sodium, medications, ionized calcium

evidence suggests that potassium is of significant hemodynamic importance during hemodialysis. In an EDTA survey, high predialysis serum potassium was associated with more frequent hypotension (15). Hypokalemic dialysis is associated with a greater fall in plasma catecholamines and a suppression of the normal heart rate response to hypovolemia compared to isokalemic dialysis (16). Postdialysis (rebound) hypertension was associated with low (1–2 mEq/L) but not high (3 mEq/L) dialysate potassium (17). Infusion of 10–20 mEq of potassium during the last 30 min of dialysis reduces intradialytic hypotension (18).

Osmolar flux also differs in daily versus thrice-weekly dialysis, a difference that might also have hemodynamic consequences. Postdialysis orthostatic hypotension occurred when isotonic mannitol was given during treatment and plasma osmolality was allowed to decline. However, orthostatic hypotension was absent (19) when the same quantity of mannitol was given in hypertonic form and plasma osmolality was kept stable during treatment. Since daily dialysis requires less osmotic flux and is associated with a more stable plasma

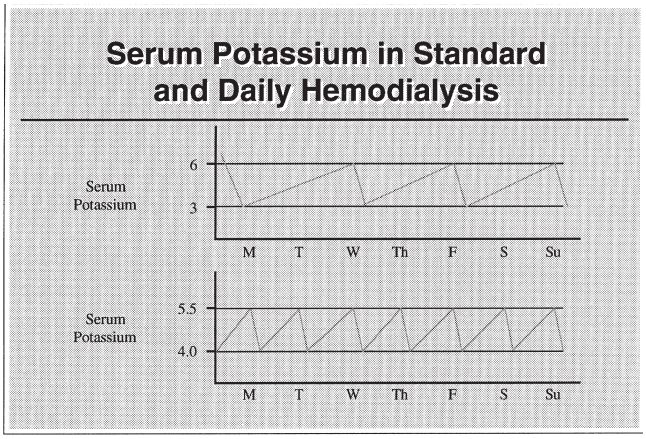

FIGURE 3 Daily therapy should be associated with smaller oscillations in plasma solute levels including potassium.

osmolality than thrice-weekly dialysis, this observation may be relevant to the hemodynamics of daily dialysis.

The interleukin hypothesis may also account for a better tolerance to daily therapy (20). This hypothesis suggests that activation of cytokines during dialysis is responsible for hemodynamic instability. Since this activation requires several hours to take place, short treatment times may protect patients from this cytokine-induced instability.

The basis for the apparent improvement in volume status and tolerance to ultrafiltration with daily hemodialysis is currently uncertain. The shorter treatment time clearly limits the extent to which plasma volume is reduced during treatment. However, the likely increase in UFR and decrease in PRR during daily treatment raises the possibility that other factors related to daily dialysis are responsible for any favorable hemodynamic effects of this therapy. The difference between daily and thrice-weekly hemodialysis in solute levels, dialytic flux, and/or cytokine effects may prove to be an important factor accounting for the (so far) limited observations that have been made.

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