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## The Case for Every-Other-Day Dialysis

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*Until daily dialysis becomes widely available, we believe that hemodialysis patients would benefit enormously from every-other-day dialysis (EODD), which may be implemented both by home patients and in centers. Benefits of EODD over the routine, three-times-weekly schedule would include decreased mortality after the weekend interval without dialysis; increased weekly dose of dialysis, resulting in better rehabilitation; and improved blood pressure control.*

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### Key words

Frequency of hemodialysis, blood pressure control, dialysis adequacy, every-other-day dialysis

### Introduction

The Bible says that God decreed the 7-day week. Unfortunately, it has not been good for hemodialysis patients. A recent study of the septadian rhythm of deaths in hemodialysis patients, based on analysis from the United States Renal Data System (USRDS), showed an uneven distribution of sudden and cardiac deaths in hemodialysis patients; whereas there was an even distribution of sudden and cardiac deaths in peritoneal dialysis patients [1]. Hemodialysis patients were more likely to die suddenly or of cardiac causes on Monday or Tuesday. It is clear from this study that the intermittent nature of hemodialysis, particularly long periods without dialysis over the weekends, predisposes to increased mortality after the weekend; whereas the continuous or quotidian nature of peritoneal dialysis does not predispose to such a phenomenon. Even if hemodialysis patients do not die on Monday or Tuesday, many feel worse on these days, particularly if they do not have residual renal function. Many patients feel short of breath before dialysis on these days, and feel particularly “washed out” after dialysis.

There is no question that the best schedule of hemodialysis is a daily hemodialysis: either short, performed in 1.5- to 3.0-hour sessions during the daytime; or long and nocturnal, where a patient dialyzes for 6 – 10 hours while sleeping. In recent years, centers in Canada, Belgium, The Netherlands,

France, Finland, Brazil, and Germany, and several centers in the United States, established daily dialysis programs [2]. All reports confirm beneficial effects of daily hemodialysis on blood pressure (BP) control, hematocrit, nutrition, mental health, energy, social functioning, physical activity, sexual function, and vitality [3–7]. However, daily hemodialysis is performed mostly at home and is not widely accessible. Because of logistic and fiscal problems, in-center daily hemodialysis is not performed, with a few notable exceptions [8,9].

We believe that, until daily dialysis becomes widely available, hemodialysis patients would benefit enormously from every-other-day dialysis (EODD), which, with minimal effort (Sunday shifts), may be implemented now at patients’ homes and in dialysis centers. First, the increased mortality after the weekend would disappear. Second, the weekly dose of dialysis would increase, alleviating the chronic uremia that prevents rehabilitation of most patients on a three-times-weekly schedule. Finally, EODD would greatly facilitate hypertension control by materially reducing the amount of ultrafiltration per session.

### The effect of EODD on dialysis dose

Dialysis dose is measured nowadays by the removal of small molecules, represented by urea. Since the large National Cooperative Dialysis Study in the mid-1980s,  $Kt/V_{\text{urea}}$  has become a standard measure of dialysis dose. In this study, the 1-year risk of hospitalization was found to be greater in patients with higher BUN. In a reanalysis of the data, Gotch and Sargent [10] concluded that  $Kt/V$  over 0.9 or 1.0 in hemodialysis does not further decrease hospitalization rates, and thus for several years a  $Kt/V$  of 1.0 was recommended as a measure of adequate dialysis. Gradually, however, reports showed that the recommended  $Kt/V$  was too low. Owen *et al.* [11] found improvement in mortality rates with a urea reduction ratio (URR) of 65% – 69% ( $Kt/V_{\text{urea}}$  of 1.2 – 1.3) compared to lower values. Based on a broad review of the available data, Hakim *et al.* [12] concluded that optimum dialysis may be achieved with a  $Kt/V_{\text{urea}}$  of 1.4 or greater. The Dialysis Outcomes Quality Initiative (DOQI) guidelines [13] recommend a  $Kt/V_{\text{urea}}$  for hemodialysis of at least 1.2.

Recent national data from the USRDS showed that the delivered dose rose over the past decade and that this increase coincided with a decrease in mortality [14]. The frequency of twice-weekly dialysis prescriptions decreased, whereas the duration of each treatment showed only minor changes. A large-scale analysis of mortality in United States chronic

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dialysis patients [15] has determined a robust inverse correlation with delivered hemodialysis dose, whether measured by Kt/V or by URR. Mortality risk was lower by 7% ( $p = 0.001$ ) with each 0.1 increase of delivered Kt/V. Expressed in terms of URR, mortality was lower by 11% with each 5-percentage-point increase in URR ( $p = 0.001$ ). These data did not provide statistical evidence of further reductions in mortality with a URR above 70% or a Kt/V above 1.3. The authors concluded from this study that the “level of hemodialysis dose measured by URR or Kt/V beyond which the mortality rate does not continue to decrease, though not well defined with this study, appears to be above current levels of typical treatment of hemodialysis patients in the U.S.” Charra *et al.* [16] did not find Kt/V to be a predictor of survival, but their patients had a mean Kt/V of 1.79. We suspect that the Kt/V level where there will be no further improvement may lie well above 1.3.

Kt/V is only one measure of dialysis efficiency. It assumes that  $t$  may be shortened with an equivalent increase in  $K$ , without detriment to the patient. Although this is true for urea, it is not true for BP control (see below). Also, short dialysis is not efficient in removing larger molecules, such as phosphate, sulfate, phenols, uric acid, and middle molecules, some of which are uremic toxins. Longer dialyses improve transfer of bicarbonate into the patient [17]. The correction of acidosis decreases protein catabolism [18].

EODD, if performed with the same duration as three-times-weekly dialysis, will increase weekly dialysis time by 16.7%. By simple summation of Kt/V, the increase in Kt/V will be also 16.7%; however, increased frequency improves doses beyond the simple summation. Gotch [19] estimates that, at the same single dialysis equilibrated Kt/V of 1.3, three-times-weekly dialysis gives a  $\text{stdKt/V}$  (equivalent to continuous clearance) of 2.3, whereas EODD (3.5 per week) gives a  $\text{stdKt/V}$  of 2.7 (an increase of 17.4%).

### The effect of EODD on control of hypertension

There is ample evidence that hypertension is almost impossible to control on the 3- to 4-hour three-times-weekly dialysis schedule in common use worldwide. This has led to an epidemic of atherosclerosis among patients on dialysis therapy [20]. EODD would dramatically improve control of hypertension by allowing much wider application of the drug-free, dry-weight method of BP control, which has been proven the only successful method of controlling hypertension in the dialysis population [21,22].

The success of the dry-weight method of BP control depends upon keeping the time-averaged extracellular volume (ECV) low enough so that the patient remains normotensive and does not have problems with hypotension during dialysis, which in turn requires sufficient dialysis time for gentle ultrafiltration to remove the ingested sodium. In the dialysis unit in Tassin, France, where the dry-weight method was perfected [23], sufficient ultrafiltration is accomplished by employing an 8-hour, three-times-weekly dialysis schedule.

This schedule does not work in the vast majority of dialysis centers, which explains, in part, why hypertension is so poorly controlled among dialysis patients worldwide.

We believe that a 3- to 4-hour EODD schedule, which could be adopted easily by most centers, would materially improve control of hypertension. First and foremost, EODD would eliminate the long, weekend interval inherent in the three-times-weekly schedule, eliminating the postweekend dialysis during which hypotensive episodes are more frequent because of the need for excessive ultrafiltration. These episodes not only make fluid removal more difficult, but further reduce the inadequate dose of dialysis inherent in current schedules. EODD would eliminate this phenomenon completely. Fluid removal during each dialysis session would become more equal, and therefore make it easier to maintain the patient at dry weight, which we define as that weight at which the dialysis patient remains normotensive off all antihypertensive medications [21–23].

We believe in BP control using the dry-weight method. This would be the case especially among patients who are able to consume less than 4 g of dietary sodium per day. EODD gives patients a better chance of becoming normotensive, thereby avoiding the horrendous atherosclerotic complications caused by hypertension in this highly susceptible dialysis population [24,25].

### Conclusion

Home hemodialysis patients in Columbia, Missouri, are already using EODD to avoid after-the-weekend postdialysis hangover and to facilitate BP control. In-center dialysis patients do not have this option, but dialyze 4 days per week if they absolutely cannot tolerate a three-times-weekly schedule.

We believe that EODD should be widely available so that both physicians and patients have this option to improve dialysis dose, blood pressure control, and survival. In return, an immediate and obvious improvement in patients' well-being would recruit more patients to EODD. Further, we believe, the increased cost would be more than offset by decreased hospitalizations and treatment of complications. Cost savings should be realized immediately because of reduction in emergency treatments of pulmonary edema on Sundays and Mondays.

Finally, no expensive, double-blind, national study would be necessary to validate EODD.

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