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Feasibility of Incremental 2 Times Weekly Hemodialysis in Incident Patients With Residual Kidney Function

Andrew I. Chin[1,2], Suresh Appasamy[1], Robert J. Carey[1] and Niti Madan[1]

[1]Department of Internal Medicine, Division of Nephrology, University of California, Davis School of Medicine, Sacramento, California, USA; and [2]Division of Nephrology, Sacramento VA Medical Center, VA Northern California Health Care Systems, Mather Field, California, USA

Introduction: We hypothesized that at least half of incident hemodialysis (HD) patients on 3 times weekly dialysis could safely start on an incremental, 2 times weekly HD schedule if residual kidney function (RKF) had been considered.

Methods: RKF is assessed in all our HD patients. This single-center, retrospective cohort study of incident adult HD patients, who survived ≥6 months on a 3 times weekly HD regimen and had a timed urine collection within 3 months of starting HD, assessed each patient's theoretical ability to achieve adequate urea clearance, ultrafiltration rate, and hemodynamic stability if on 2 times weekly HD.

Results: Of the 410 patients in the cohort, we found that 112 (27%) could have optimally and 107 (26%) could have been appropriately considered for 2 times weekly incremental HD. In general, diuretics were underutilized in > 50% of subjects who had adequate RKF urea clearance. The optimal 2 times weekly patients had better potassium and phosphorus control. The correlation coefficient of calculated residual kidney urea clearance with 24-hour urine volume and with kinetic model residual kidney clearance was 0.68 and 0.99, respectively.

Discussion: More than 50% of incident HD patients with RKF have adequate kidney urea clearance to be considered for 2 times weekly HD. When additionally ultrafiltration volume and blood pressure stability are taken into account, more than one-fourth of the total cohort could optimally start HD in an incremental fashion.

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In the United States, most individuals who begin long-term hemodialysis (HD) do so on a 3 times weekly prescription. About 40% of incident patients begin HD with an estimated glomerular filtration rate (GFR) of ≥ 10 ml/min,[1] and this possibly suggests that many patients have substantial residual renal function (RKF). Indeed, a good proportion of incident patients have meaningful RKF at the time of HD initiation when it is measured.[2] In addition to native kidney urea clearance (K_{RU}), RKF also augments weekly volume removal, improves electrolyte balance, lowers erythropoietin-stimulating agent requirement, and provides clearance of protein-bound solutes and middle molecules.[3,4] Most importantly, there is a large positive and robust relationship between RKF and HD patient survival.[5–7]

Correspondence: Andrew I. Chin, 4150 V Street, Suite 3500, Sacramento, California 95817, USA. E-mail: aichin@ucdavis.edu
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Although guidelines on HD adequacy briefly mention the possibility of adjusting the HD prescription to take into consideration K_{RU}, adjusting the frequency of HD is either not directly addressed or is mentioned only in brief.[8,9] If we applied the concept of incremental HD, the tailoring of the prescription to complement the amount of RKF, perhaps some patients could do well on a less than 3 times weekly HD schedule. It is not known how many incident HD patients in the United States could start HD incrementally, because few incident HD patients ever perform a timed urine collection; in some cohorts, < 5% of HD patients ever have a formal evaluation of RKF.[10]

It is our standard practice to obtain 24-hour urine collections in all HD patients. Timed urine collections are performed within the first 3 months of starting dialysis and then every 3 months thereafter, until either the patient reports no significant urine production or a 24-hour urine collection reveals < 100 ml of volume. We have used the K_{RU} information primarily

to adjust the duration of dialysis; most patients are on 3 times weekly HD. With extensive RKF data, we are uniquely positioned to determine the theoretical feasibility of incremental start HD across incident HD patients.

Our specific aim was to estimate how many incident HD patients could have started HD on a 2 times weekly instead of a 3 times weekly basis. In this theoretical assessment, we determined that an optimal 2 times weekly HD patient would need to meet the following criteria: (i) adequate weekly total (kidney plus dialyzer) urea clearance; (ii) ultrafiltration (UF) rate $\leq$ 13 ml/kg/h per dialysis; (iii) stable blood pressure on HD; and (iv) minimal side effects such as nausea and vomiting while on dialysis. In addition, we used a 4-hour per HD treatment time limit in the calculations. Even with these conservative constraints, we hypothesized that the majority of clinically stable incident patients who continue to make urine could have started very safely on HD in an incremental 2 times weekly fashion.

MATERIALS AND METHODS

Study Subjects

In this single-center, retrospective cohort study, we analyzed all incident adult patients on 3 times weekly HD, who were admitted to 4 dialysis clinics over 14 years, and who survived $\geq$ 6 months and had K_{RU} measured within $\leq$ 3 months of starting HD. Incidence was defined as receiving a first ever in-center HD treatment within $\leq$ 3 months of the first dialysis treatment date listed. Patients were excluded if they had prior renal transplantation, were discharged from the clinic for any reason, received $<$ 75% of the expected in-center HD treatments, died $<$ 6 months after their first HD treatment, were not initially prescribed a treatment frequency of 3 times weekly, or did not have a 24-hour urine collection within the first 3 months. Data were queried from the dialysis unit database. This study was approved by the Institutional Review Board of the University of California, Davis, as well as by the administrative review board of the dialysis provider (Dialysis Clinic, Inc.).

Patient Data

Demographic information included age, race, ethnicity, gender, and cause of renal failure. For each patient, HD parameters within the first 3 months included treatment times, pre- and post-HD blood pressures, blood flow rates, dialysate flow rates, type of vascular access (the one used for the majority of the time), pre- and post-HD weights, medications given on HD, and adverse symptoms while on dialysis (nausea, vomiting, cramps, or hypotension).

Urine collection data were obtained within 3 months of the in-center HD start date, and included volume, day of the week of collection, and urea concentration. Urea clearance calculation was based on the blood tests done on the next day. All other laboratory information was averaged from the first 3 months. Kinetic modeling data, for the first 3 months, included volume of distribution of urea (V), modeled dialyzer clearance (K_d), urea generation rate (G), and single pool per treatment clearance (spKt/V). Medications were noted for angiotensin-converting enzyme inhibitors, angiotensin receptor antagonists, and diuretics (furosemide, torsemide, bumetanide, hydrochlorothiazide, chlorthalidone, metolazone, spironolactone, and eplerenone).

Urea Clearance Criterion

We chose to utilize the which is based on the concept of a stable mean predialysis blood urea nitrogen (BUN) concentration, to add K_{RU} to the dialyzer clearance.[11] Standard weekly clearance is a well-established method of assessing dialysis adequacy and allows the addition of clearances obtained from various methods.[8,12] Using explicit equations, the per-session dialyzer single pool clearance (spKt/V) was converted into a continuous weekly equivalent clearance, stdKt/V(dialysis). We used a modified Tattersall equation with a time constant of 30.7 minutes[13] to convert spKt/V into an equilibrated value (eKt/V), where "t" is the dialysis duration in minutes:

$$\mathrm{eKt/V} = \mathrm{spKt/V} \times \left(\frac{\mathrm{t}}{\mathrm{t}+30.7}\right) \quad (1)$$

The next step utilized the simplified equation for standard weekly clearance:

$$\mathrm{stdKt/V} = \frac{10080 \times \frac{1-e^{-\mathrm{eKt/V}}}{\mathrm{t}}}{\frac{1-e^{-\mathrm{eKt/V}}}{\mathrm{eKt/V}} + \frac{10080}{\mathrm{F}\times\mathrm{t}} - 1} \quad (2)$$

where "F" is number of HD treatments per week and "t" is treatment time. Equation 2 is based on a single-pool, fixed-volume model with no volume removal. Although both spKt/V and eKt/V do theoretically account for convective clearance of urea during ultrafiltration, the effect is not complete when converting the per-session clearance to a standard weekly clearance. We used a correction that was recently published in order to take into account the additional convective urea clearance obtained by dialysis volume removal.[13] Therefore, the final standard weekly clearance obtained by the dialyzer is:

$$\mathrm{stdKt/V(dialysis)} = \frac{\mathrm{S}}{\left(1 - \frac{0.74}{\mathrm{F}} \times \frac{\mathrm{UF_w}}{\mathrm{V}}\right)} \quad (3)$$

where "S" is the result equation 2, "F" is again the number of HD treatments per week, "UF_w" is the weekly volume removed by HD expressed in liters, and "V" is the volume of