Core Curriculum

Prescribing and monitoring hemodialysis in a 3-4 ×/week setting

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Abstract
The basics of targeting, writing, adjusting, and monitoring a hemodialysis prescription are reviewed for patients being dialyzed 3 or 4 times a week. K/DOQI 2006 adequacy guidelines and practice recommendations are reviewed, and a practical method using a variety of nomograms is suggested to monitor and adjust the desired level of Kt/V.

Key words: Hemodialysis, adequacy, Kt/V, dialyzer, urea, modeling

INTRODUCTION
One of the challenges for nephrologists is to ensure an adequate amount of dialysis for their patients. In a practical sense, the tasks include:

(a) Targeting an initial prescription.
(b) Writing an initial prescription.
(c) Adjusting the prescription to achieve a desired urea reduction ratio (URR) or Kt/V.
(d) Monitoring dialysis adequacy of groups of patients.

Targeting the initial prescription
With regard to the initial prescription for a 3 ×/week patient, what is the goal? We have K/DOQI to inform us that the minimum dialysis dose should be 1.2 Kt/V units (single-pool) and that the minimum target should be 1.3.1 In the clinical practice recommendations, more information is available, although not supported by hard evidence. The most important of these include (a) consideration of higher Kt/V targets for smaller patients and for women, and (b) a limited reduction of the required minimum targets for patients in whom residual renal function exceeds 2.0 mL/min/1.73 M². The spKt/V targets for 3 ×/week dialysis are not appropriate for more frequent dialysis, and using the “standard Kt/V” concept developed by Gotch,2 the K/DOQI work group recommended lower minimum targets for dialysis being given 4 ×/week1 as well as for other schedules.

Writing an initial prescription
The Kt/V components are K, the dialyzer clearance, t, the session length, and V, the patient’s urea distribution volume, which is similar in size to the total body water.

Empiric approach to the dialysis prescription
One approach, not freely admitted, but probably practiced by a great many excellent nephrologists, is to place dialysis patients on the largest dialyzer that they can afford, and to dialyze patients for the longest amount of time that the patient will agree to and with the highest blood flow rate that the vascular access will deliver. Then, to check the URR and/or Kt/V, and if deficient, to attempt to take some sort of corrective action.

Because K will tend to be similar for all patients, as well as t, the Kt/V will depend inversely on the patients’ body water volume. So this empiric approach will result in higher Kt/V values for patients with small Vs, including women. It will also result in lower Kt/V values for large patients, and especially for large male patients with high amounts of muscle.
An alternative approach, the so-called formal “modeling” approach, is to attempt to prescribe a specific Kt/V value using an anthropometric estimate of the patient’s volume, and dialyzer clearance values from either a modeling program or a nomogram, based on dialyzer KtA, blood flow rate, and dialysate flow rate. Usually people attempt to target a Kt/V value well above the K/DOQI prescribed minimum value of 1.2, and usually target in the range of 1.5 or so.

Practically, after a few iterations, the two approaches yield very similar results. In the smaller patients, including most women, a minimum spKt/V of 1.5 is achievable. For the larger patients, such values are achieved to greater or lesser degrees of success, and for the largest patients, spKt/V values tend to fall short, often being in the 1.0 to 1.1 range.

Two issues are pertinent here: Although the K/DOQI adequacy work group, in their 2006 guidelines recommends a minimum of 1.2 spKt/V for all 3 × /week patients, in the clinical practice recommendations, it is suggested to give higher amounts of dialysis to smaller patients and for women. These recommendations are based on the HEMO trial evidence of a poorer outcome for women randomized to the standard dose group (in whom spKt/V was close around 1.3), and the generally poorer outcome of hemodialysis patients with lower values of V in observational studies (see discussion in Hemodialysis Adequacy 2006 Work Group). So the take-home message here is, if one does prescribe dialysis using modeling, it may not be appropriate to target doses close to 1.2 to 1.3 in small patients and especially not in women. This first issue is not really a problem, since small patients and women “naturally” are prescribed doses of dialysis close to about 1.5.

A second issue is more difficult. Whether one uses an empirical or a prescriptive approach, the end results with large male patients are often similar—a spKt/V that does not reach the K/DOQI mandated minimum value of 1.2. In such patients, the V is so large, that often 5 hr of dialysis and/or use of 2 dialyzers in tandem or an ultra-high efficiency dialyzer is needed to achieve the minimum recommended dose. Is this additional effort really necessary for these very large patients? No one really knows. The HEMO study excluded such patients, since all patients were tested to be able to achieve a spKt/V of about 1.7 before randomization. Such very large and muscular patients tend to do well overall, despite their lower Kt/V dose. Their mortality does depend on Kt/V in observational analyses, but much of this apparent signal could be due to “dose-targeting bias”.

What are the steps to take for an initial dialysis prescription?

**Step 1: Find the desired spKt/V**
One can target either an spKt/V or a URR. K/DOQI recommends targeting and measuring Kt/V. One needs to realize that the amount of fluid removed per session divided by a patient’s V (UF/V), or fluid removed divided by a patient’s weight (UF/W) will result in noticeably different values of Kt/V for similar values of URR (Figure 1). The reasons for this are explained in detail elsewhere.

Assume that a URR of 0.75 (75%) is being targeted
To find the desired Kt/V, one can use the nomogram depicted in Figure 1. First, find 0.75 on the y-axis. Next, move to the right until you intersect the proper line corresponding to the amount of fluid being removed. Then drop down to the x-axis to read off the Kt/V. For example, if no fluid is being removed, to achieve a URR of 75%, a Kt/V of 1.5 will be required. If 6% of the body weight is being removed (say 0.06 of 70 kg = 4.2 kg per treatment), then a Kt/V of 1.7 will be required.

**Step 2: Estimate the patient’s urea distribution volume (V)**
This can be done using calculators and the Watson equation, or using a simple nomogram (Figure 2a,b). The nomograms are based on a related equation, by Hume.
and Weyers.\textsuperscript{8} It is important to examine these nomograms closely in order to realize to what extent the urea distribution volume is a function of both height and gender. For example, if we consider Estimated V (from Hume-Weyers Nomogram, Figure 2a,b):

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Height (inches, cm)</th>
<th>Men</th>
<th>Woman</th>
</tr>
</thead>
<tbody>
<tr>
<td>60 kg, 5’0” tall</td>
<td>100-110</td>
<td>33 L</td>
<td>29 L</td>
</tr>
<tr>
<td>60 kg, 6’0” tall</td>
<td>120-130</td>
<td>40 L</td>
<td>34 L</td>
</tr>
</tbody>
</table>

So, 4 patients, all having a weight of 60 kg, are predicted to have markedly different urea volumes, ranging from 29 to 40 L. This means that a 60 kg, 6-foot tall male patient will receive 40/29=1.38, or 38% more dialysis than a 60 kg, 5-foot tall woman. This is because urea distribution volume is tied to muscle mass, and men have more muscle mass than women of same height and weight, and for both sexes, taller people tend to have more muscle mass than shorter people. Whether or not dialysis dose should be sized to urea distribution volume is a matter of current controversy. Sizing dialysis to body surface area\textsuperscript{9}\textsuperscript{10} is an alternative method, but which has not been recommended by K/DOQI, perhaps due to the newness of the approach, and the limited outcomes evidence available.\textsuperscript{9} However, the finding in the NIH HEMO trial, that women tended to do better on the higher dose of dialysis,\textsuperscript{3} and the finding in observational studies, that smaller patients do poorer than larger patients,\textsuperscript{11} led to clinical practice recommendations in the 2006 version of the K/DOQI guidelines, to give more dialysis to smaller patients and to women (K/DOQI). In any case, assume that our patient is a woman weighing 60 kg, who is 5-feet tall. The Hume-Weyer nomograms tells us that her estimated V will be around 30 L, and so we will develop our target prescription for such a 30-L patient.

**Step 3: Estimate the K \times t**

Now we are simply discussing algebra. From Step 1, we wanted a URR of 75%, and so a Kt/V of either 1.5 or 1.7, depending on the UF rate. For simplicity sake, let us target a Kt/V of 1.6. So this means that the (K \times t), or the numerator, needs to be 1.6 times the denominator (V), or 1.6 \times 30=48 L, or 48,000 mL.

**Step 4: Set the dialysis session length (t)**

The dialysis session length is important not only in terms of urea removal, but also in terms of salt and water removal and phosphate removal. In some observational

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\textbf{Figure 2} (a) Nomogram showing estimated urea distribution volume (as total body water) for men, according to Hume and Weyers.\textsuperscript{8} (b) Nomogram showing estimated urea distribution volume (as total body water) for women, according to Hume and Weyers.\textsuperscript{8}
results, notably in DOPPS data, longer session lengths have been linked to increased survival.\textsuperscript{12} The K/DOQI clinical practice guidelines recommend a minimum session length of 3.0 hr for 3/week schedules in patients with little residual renal function.\textsuperscript{1} So let us set the session length at 3.0 hr and 20 min, which of course, is equal to 200 min.

**Step 5: Calculate the required dialyzer clearance value (K)**

To get the required value for K, we simply divide the Kt term of 48,000 mL by t (200 min). This gives us a required clearance of 240 mL/min. Now the next step is to see how we can achieve this. For this, we look at Figure 3a,b. These give estimated dialyzer clearances as a function of blood flow rate and dialyzer efficiency (K0A). Figure 3a is for a dialysate flow rate of 500 mL/min, and Figure 3b is for a dialysate flow rate of 800 mL/min, where, for rapid blood flow rates, clearances are about 10 to 15% higher.

It is best to start with the blood flow rate, since this will be limiting in most patients. Assume that we know we can get a blood flow rate of 400 mL/min in this patient. We first go to Figure 3a, find 400 on the x-axis, and then move up through the different dialyzers. The dialyzer efficiency is listed in terms of “mass-transfer area coefficient,” or K0A. The K0A, or “mass-transfer area coefficient” is actually a clearance, and is the theoretical maximum clearance for that dialyzer and infinitely high blood and dialysate flow rates. Most high-efficiency dialyzers in use today have a K0A in the 1000 to 1200 mL/min range. So we see, from Figure 3a, that a dialyzer with a K0A of 1000 will, in fact, result in an estimated clearance of about 240 mL/min. This assumes, of course, that the blood flow rate of 400 mL/min can be reliably delivered throughout the treatment.

So now we write our prescription:

Dialyzer K0A = 1000 mL/min (choose the appropriate dialyzer);
Qb (blood flow rate) = 400 mL/min;  
Qd (dialysate flow rate) = 500 mL/min;  
Session length = 200 min.

Adjusting the prescription based on URR

The next step is to dialyze the patient and then measure the URR and determine what Kt/V is being achieved. Again, this depends on how much fluid is being removed per treatment. We can use the nomogram in Figure 1 to accomplish this. For example, if the URR values for January, February, and March are all close to 75%, and if we are removing about 3% of the body weight (0.03 \times 60 kg = 2.4 kg per treatment), then a Kt/V of 1.6 is indeed being achieved, and we have nothing further to do.

If the URR is higher, say 80%, this corresponds to a spKt/V of about 1.9. This can happen, since the true urea distribution volume of the patient may be smaller than estimated from the Hume-Weyers nomograms. In such a case, I probably would leave the patient on the same treatment schedule.

On the other hand, if the URR is consistently below target, say about 70%, then from Figure 1, the Kt/V is estimated to be about 1.4. We can either accept this, or if we want to increase it to 1.6, we know that we need more dialysis. How much more? Simply divide 1.6/1.4 = 1.14; so we need 14% more “K x t.” How can we deliver 14% more dialysis? We have several options. The first is to increase the session length (t). The current session length of 200 min can be thought of as somewhat borderline, particularly in someone with little residual renal function. So we can increase this by 14%, 1.14 \times 200 min = 230 min. Thus, if we add 30 min to the session length, then we should be done. K x t will increase by 14%, and Kt/V will also increase, bringing the patient up from 1.4 to 1.6.

Another way to increase the K x t is to increase the clearance, K. We need an increase in clearance of 14%. So, the previous clearance of 240 needs to be multiplied by 1.14 \times 240 = 274 mL/min at a 200-min session length for this patient. To do this, we examine the clearances shown in Figure 3a,b. If we use a dialysate flow rate of 800 mL/min, we can expect a clearance of about 276 mL/min instead of 240 with the same K0A = 1000 dialyzer. So this is a 14% increase. You can see from Figure 3a, that if we keep dialysate flow rate at 500 mL/min, increasing the blood flow to 450 mL/min will only get us up to a clearance of 250 mL/min, which would not be enough. What about a bigger dialyzer? We see from Figure 3a that going up to the largest dialyzer available, with a K0A of 1600 mL/min (and many of the factory-supplied figures are a bit overestimated), might get the clearance up to the required 275 mL/min. In practice, a combination of modifications can be made, such as, increasing time, increasing dialysate flow rate, increasing blood flow rate, or moving to a bigger dialyzer.

When the URR falls

What happens if one gets URR values of 75, 75, 75, and then suddenly, 60%? Clinical judgement is required. The variability in the URR on sequential measurements tends to be high, so prescription changes are best made on the basis of a running average of sessions. A sudden drop in the URR is most often due to some problem with that particular session around which the URR was measured, including some technical problem requiring stopping dialysate flow, reducing blood flow, or shortening the session length. Access recirculation or reversing of the dialysis needles must also be considered; and the solution ultimately may require access revision.

When the URR suddenly rises

These most often are due to technical errors. If there is a very marked rise, it probably is due to postdialysis blood being drawn from the dialyzer outflow line instead of the inflow line. Another common cause is in a patient with access recirculation. One time the blood is drawn properly, after a short slow-flow period, to properly remove recirculated blood from the sampling area. This results in a “true” URR. If the postdialysis blood is not drawn using a slow-flow period, for example, if the blood flow is simply stopped, then if access recirculation is present, partially recirculated blood may be sampled. The true postdialysis BUN is higher than measured, and the URR is overestimated. In all such cases, staff must be carefully questioned about how the postdialysis blood is being drawn, since there is no other way to detect such an error.

Monitoring adequacy for patients across the whole unit

K/DOQI recommends that some sort of quality control and assurance program be in place to monitor dialysis adequacy in the patients as a group. In units reusing dialyzers, this can pick up problems with dialyzer reuse such as insufficient heparinization, which can lower dialyzer clearance. Other simple issues can be detected, such as a substantial number of patients signing off early. Problems in blood roller pump calibration, tensioning, and prepump pressure-induced collapse of less-than-optimal dialyzers.
timal blood lines can also be detected in this manner. Complex statistical methods are not needed, but the software does require the ability to track URR results in groups of patients over time. Because the URR values will change with changes in prescription, one can standardize QA monitoring by computing the “modeled V” for dialysis patients. Basically, from the URR and weight loss, the modeling program estimates the Kt/V. Then the program uses the values for K and t to compute the volume of blood cleared, Kt. From the URR, and the Kt, the computer can predict the “size” of the box from which urea is being removed. For a given Kt, if the URR is high, this predicts a small patient, and if the URR is low, then this predicts a larger patient. Think of removing a certain number, say 5, of fish from a tank. If the concentration of fish drops by 50%, you have a small tank. If the concentration drops by only 1%, then you have a very large tank. So a kinetic modeling program will compute a modeled volume (Vmod) for each patient that should be relatively independent of the particularities of that patient’s dialysis prescription. The value of Vmod is only as good as the information being entered. So the values for dialyzer clearance K (which depends on Qb, Qd, and K0A) and session length (t) all need to be entered properly. One can then estimate the value for V using either the Watson equation or some other nomogram, and compute the ratio of Vmod/Vant (modeled to anthropometric) across all patients for each URR sampling date, and then follow this over time for the entire unit.

CONCLUSIONS

Using basic principles of urea modeling, it is quite easy to come up with an initial dialysis prescription, to adjust the prescription to achieve desired adequacy targets, and to monitor patients in the unit to ensure that the desired adequacy strategy is being implemented, and to identify quality control issues with the dialysis procedure.

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REFERENCES