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The Hemodialysis Product (HDP): A Better Index of Dialysis Adequacy than Kt/V

In a recent issue of this journal, Dr. Peter Blake and others commented on the ADEMEX (Adequacy of Peritoneal Dialysis in Mexico) study, a brilliantly planned and conducted study on the influence of increases in Kt/V on the outcome of anuric continuous ambulatory peritoneal dialysis (CAPD) patients in Mexico.[1] This prospective, controlled study was presented at the recent meeting of the International Society for Peritoneal Dialysis (Montreal, June 2001), but has not yet been published.

The results were clear-cut and highly significant. Specifically, they demonstrated that increasing the dose of CAPD—as measured by Kt/V and weekly creatinine clearance—among anuric CAPD patients had no effect on patient survival when compared to a control group on a lower dose of dialysis.

This result provides additional evidence that Kt/V is a flawed concept upon which to base the dose of dialysis in general. The prime example that Kt/V is flawed is that it fosters short hemodialysis, which is inefficient in removing toxic middle molecules. Short hemodialysis may give a false impression of highly efficient hemodialysis by removing fast-diffusing urea and, thus, resulting in a high Kt/V. However, removal of toxic middle molecules and PO_4, which dialyzes like a middle molecule, is reduced because of the shortened time. Short hemodialysis sessions have great appeal only to the uninformed dialysis patient and to for-profit dialysis centers.

For the last three decades worldwide, but especially in the U.S.A., belief among the hemodialysis community in the reliability of Kt/V, combined with the natural desire of the patient to have the shortest possible time on dialysis, has resulted in the underdialysis of the vast majority of hemodialysis patients.[2]

Validating the Middle Molecule Hypothesis

For decades, it has been abundantly clear that many important uremic toxins have a much larger molecular weight than does urea. The first hint of this came in Seattle during the early 1960s when Scribner observed that patients on chronic peritoneal dialysis seemed to be healthier than hemodialysis patients, despite less dialysis (as measured by creatinine clearance).[3] This, in turn, led to the brilliant formulation by Babb of the middle molecule (MM) hypothesis.[4,5]

Out of this formulation, Babb et al. predicted that the peritoneum cleared MMs better than did the early dialysis membranes, which proved to be the case.[6] Despite this finding, the improved well-being of the early Seattle PD patients may have been due, in part, to better preserved residual renal function, as Bargman et al. recently pointed out.[7]

The ADEMEX study provides further support for the much ignored MM hypothesis by demonstrating that the techniques that lead to increased urea removal did not improve patient health and well-being; rather, they caused harm to the CAPD patients due to increased exchange volumes. If the authors had followed a middle molecule marker during the study, perhaps they could have predicted the outcome long before the study was completed.

There is irrefutable support for the conclusion that it is the adequate removal of middle molecules, rather than the removal of urea, that correlates with survival and well-being among patients on hemodialysis. An important part of this evidence comes from the results obtained from more than 1,000 patients

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Table I. Various values of the Hemodialysis Product (HDP), as well as the corresponding expected clinical findings.

Hours per Dialysis Session	Dialysis Sessions per Week	HDP*	Clinical Results
3	3	27	Totally inadequate. Severe malnutrition.
4	3	36	Inadequate. A high percent of the U.S. dialysis population is malnourished.
5	3	45	Borderline. Some malnutrition, BP control difficult.[8-12]
8	3	72	Only 3 days/wk schedule has proven to be adequate.[8-12]
5	4	80	No data yet available.
3	5	75	No data available. BP control should be easy.
2–3	6	72–108	Preliminary data: Good well-being. BP control possible if sodium intake is limited.
8	6	288	Best so far because PO_4 normalized. BP control very easy.[16,17]

**Hemodialysis Product = (hours/dialysis session) x (dialysis sessions/week)^2*

studied over the past 30 years in the dialysis program in Tassin, France,[8-12] where the survival of HD patients is the best in the world. These results correlate with middle molecule removal as measured by the dialysis index,[5] but not with Kt/V.[8-12]

Nonetheless—for reasons that remain unexplained—the world hemodialysis community, especially in the U.S., has for two decades continued to ignore the spectacular results obtained in Tassin.

The Hemodialysis Product

Based on published evidence from many sources, we propose a new index of adequacy of hemodialysis, to be called the Hemodialysis Product (HDP). This new index incorporates dialysis frequency, which is an important variable:

HDP = (hrs/dialysis session) x (sessions/wk)^2

Table I lists various values of the HDP for average-sized adults, as well as the corresponding expected clinical results. Since the HDP does not take patient size into account, large adults will require a higher HDP, especially in the critical range below 60.

By incorporating dialysis frequency, the HDP takes into account the very positive results that have been obtained with more frequent dialysis. Again, for reasons unknown, these remarkable results have been largely ignored by the U.S. hemodialysis community.

By incorporating dialysis frequency, the HDP takes into account the very positive results that have been obtained with more frequent dialysis by De Palma,[13] Buoncristiani,[14] Bonomini,[15] Pierratos,[16] and Lockridge.[17] Again, for reasons unknown, these remarkable results have been largely ignored by the U.S. hemodialysis community, which still bases its definition of minimum adequate dialysis on a Kt/V = 1.2 per dialysis 3x/wk. Even at the latest National Institutes of Health (NIH) conference on this subject last April, the conferees chose to defer action for several years until yet another NIH-sponsored national study can provide "evidence-based results" that it is worthwhile to increase the dose of dialysis.

The HDP is a simple-to-comprehend index that already has been validated. A key example is the value of 3x/wk for 8 hours = 72. This entry represents the 30-year Tassin survival experience, which is the best in the world.[8-12] As for the lower values in *Table I,* the corresponding high incidence of malnutrition and death[2] provides the validation that these low values represent inadequate dialysis. Validation of the efficacy of the higher values, largely ignored until recently, has been going on for decades.[13-17]

Advantages of the HDP

The HDP has three important advantages over Kt/V and URR as guides to an effective dose of dialysis.

First, the HDP does not depend on any test, while Kt/V depends on blood tests that tend to err toward a falsely high value. The HDP assumes that the dialysis being given is basically sound, and—unlike the current standard for Kt/V, which is set at 1.2—has a built-in margin of safety. Still, it will be necessary to occasionally check the A-V difference of some dialyzable molecule to be sure that there is no serious recirculation taking place in the blood access.

Second, the HDP is easy for patients to comprehend. Patients can calculate and keep track of their own HDP until they can learn to judge by the way they feel whether they are receiving enough dialysis. For experienced dialysis patients who have had a high enough dose of dialysis to really regain a sense of well-being—such as those with an HDP above 70—"how they feel" is the simplest, most reliable guide of all.

The third advantage of the HDP is that the higher the value, the better the chance of obtaining BP control using the dry weight method. This method is the only way available to control hypertension in the dialysis patient. That the dry weight method is little used is evidenced by the epidemic of hypertension present among dialysis patients.[18] The proven success of the dry weight method of BP control has been clearly demonstrated.[8-12,16,17]

Increasing the Dialysis Dose

Finally, a word about the need for further evidence-based, prospective clinical trials regarding the need to increase the dialysis dose, as proposed at the recent NIH conference. The HDP concept renders further such trials unnecessary. Furthermore, as exemplified by the current Hemo Study, such trials run the risk of causing serious harm to patients in the control limb, as we believe will become apparent later this year when the results are published at the completion of that study.

In contrast, further validation of HDP values in the range of 50–70 can be obtained without undue risk and at low cost, if a regional reporting system is set up to tabulate clinical results in patients receiving doses of dialysis in this range.

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