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Achieving adequate peritoneal dialysis

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Introductory Comments

Maiorca and colleagues have recently reviewed their own experiences and the literature relative to comparisons of outcomes over many years with continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis [1]. They present evidence that control of anemia, blood pressure, cardiac function, renal bone disease, beta-2-microglobulin and uremic neuropathy are similarly controlled by the two methods when properly applied. Although the dropout rate from CAPD is higher than that from hemodialysis, patient survivals in similar patient populations are essentially identical. In centers using the Y-set to reduce peritonitis rates, differences between hemodialysis and technique survivals are much less.

Although it is difficult to quantitate, some of the dropouts from CAPD most likely reflect a failure to adjust the peritoneal dialysis prescription to appropriately provide enough weekly clearance of toxic solutes relative to the peritoneal transport characteristics and the residual renal function. If this is done, there is good evidence to suggest that patients will be as free or freer of uremic symptoms as any well dialyzed hemodialysis patient.

Well dialyzed patients should feel well, have blood pressure well controlled, have a stable lean-body mass, an hematocrit over 25 % without androgens or erythropoietin, and a stable nerve conduction velocity. They should be free of anorexia, astheny, nausea, emesis, dysgeusia and insomnia. In the peritoneal dialysis population in our program, we like to see serum creatinine concentration controlled at less than 20 mg/dl in muscular patients and less than 15 mg/dl in non-muscular patients. In our anecdotal experience, adequate peritoneal dialysis by the above criteria is usually associated with a total weekly creatinine clearance per 1.73 square meters of body surface area of 40-50 liters per week. This represents 5.8-7.2 liters of creatinine clearance per day per 1.73 square meters of body surface area. This is not to say that creatinine is incriminated as a uremic toxin, but simply to note that in our experience, clinical outcomes can be correlated with the amount of creatinine clearance provided as a useful marker. The total clearance also includes the residual renal creatinine clearance.

In patients with no residual renal CAPD, the required drain volume per day to achieve the clearance range desired varies depending on the dialysate/plasma creatinine (d/p Cr) concentration of the mixed total drain volume. Patients with d/p Cr values of 0.48-0.60 need 12 liters per day of drainage per 1.73 square meters of body surface area. A total drain volume of 10 liters per day is necessary for patients with the same average surface area and with an overall average d/p Cr of 0.58-0.72. Patients with a d/p Cr of 0.73-0.90 can do well even without renal function with only 8 liters of drain volume per day per standard body surface area.

We have found the peritoneal equilibration test very helpful in developing the prescription for a given patient while on CAPD and even for selecting those that may do better on other forms of peritoneal dialysis than CAPD.

Utilizing the Peritoneal Equilibration Test

A technique for performing a standardized peritoneal equilibration test has been published and will briefly be summarized herein [2, 3]. The study exchange consists of a two liter 2.5 % dextrose exchange in the supine position. After a preceeding exchange of 8-12 hours and complete drainage thereof, the study exchange is instilled at 400 ml/2 minutes. Ad well time of precisely four hours is allotted. Ambulation is permitted during the dwell period. Drain time in the vertical position is precisely twenty minutes. The total exchange time is 4.5 hours. Immediately after instillation and after two hours of dwell, 200 ml of dialysate is drained into the bag, mixed well and a sample taken for chemistries; the remainder is reinfused. A blood sample is drawn after two hours of dwell time. After four hours of dwell time and drainage, the dialysate is well mixed and samples taken for chemical determinations. In the standard test, glucose and creatinine concentrations are measured in all samples. Chemistries should be run on fresh or refrigerated samples. If frozen, they must be thawed for

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Table I. Peritoneal equilibration test results (2 l, 2.5 % dextrose, 4 hr dwell, n = 103)

Dialysate/plasma corrected creatinine

Minimal	Mean−SD	Mean	Mean+SD	Maximal
0.34	0.50	0.65	0.81	1.03 *

Dialysate glucose/dialysate glucose at 0 dwell time

Maximal	Mean+SD	Mean	Mean−SD	Minimal
0.61	0.49	0.38	0.26	0.12

Drain volumes (ml) after 4 hr dwell

Maximal	Mean+SD	Mean	Mean−SD	Minimal
3226	2650	2368	2085	1580

(Note that minimal d/p Cr is associated with maximal D/D_o glucose and drain volumes and the sequences are arranged so that vertical columns are the expected matched values.)

* Equilibrated value can exceed 1.0 since serum concentrations are not corrected to concentrations in serum water.

Table II. Classification of patients based on the peritoneal equilibration test

Transport	d/p Cr	D/D_o glucose	Drain volume (ml)
Low	0.34 to 0.50	0.61 to 0.49	3226 to 2650
Low average	0.51 to 0.65	0.50 to 0.38	2651 to 2368
High average	0.66 to 0.81	0.39 to 0.26	2369 to 2085
High	0.82 to 1.03	0.27 to 0.12	2086 to 1580

Table III. BUN control in hemodialysis and CAPD

Weekly kt/v	Pre-Dial	Post-Dial	Time-Average
Hemodialysis *:			
3 ***	79;66;62	31;26;24	47
1.7 ****	111;101;96	66;60;57	81
CAPD **:			
1.7	80	80	80

* Dialysis M, W, F; 42 l TBW; 56 g urea N removal/wk.
** 10 l drainage/day; 42 l TBW; 56 g urea N removal/wk.
*** 180 min M, W, F; Curea 233 ml/min.
**** 180 min M, W, F; Curea 130 ml/min.

two hours at 37° Celsius and mixed vigorously before the measurements. Creatinine concentrations must be corrected for glucose interference. The d/p Cr values are calculated at 0, 2 and 4 hours of dwell time. Concentrations of dialysate glucose at 2 and 4 hour dwell times are divided by dialysate glucose at 0 dwell time.

Mean results after four hours of dwell time are summarized in table I for d/p Cr and dialysate glucose after 4 hours to dialysate glucose at 0 dwell time (D/D_o glucose) from over 103 peritoneal equilibration tests. Table 1 indicates mean values, minimum values, maximum values, and values at ± 1 standard deviation from the mean. Table I also indicates mean drainage volumes for each of the D/D_o glucose results indicated.

Table II arbitrarily defines four groups of patients as high transporters, high average transporters, low average transporters, and low transporters based on the four intervals between the five vertical columns in table I. Note that the high transporters have high d/p Cr values and low D/D_o values. The four categories of transport also indicate the expected drain volume.

Each of the four transport groups may do fine on standard CAPD with four-2 liter exchanges per day as long as residual renal function compliments dialysis clearances and ultrafiltration. As residual renal function declines, high transporters will exhibit good peritoneal clearances but poor ultrafiltration because of the rapid glucose absorption. These patients may do better on short-cycle techniques such as nightly intermittent peritoneal dialysis (NIPD) with multiple short cycles. High transporters usually do well on NIPD with 8 to 10 hour sessions using 10-15 liters of dialysis solution nightly. Patients who fall in the high average category usually will continue to do well on CAPD in terms of daily clearances and acceptable ultrafiltration. Those with low average transport characteristics will have good ultrafiltration but weekly creatinine clearances may fall below the 40 liters per week as residual renal creatinine clearance declines. Some of these patients may need high dose peritoneal dialysis such as CAPD with at least 9 liters of instilled dialysis solution per day. Such patients with low average transport on CAPD may need more than 8 liters of dialysis solution overnight and/or more than two liters during the daytime. Patients in the low transport category have excellent ultrafiltration due to slow glucose absorption and prolonged osmotic gradients but their clearances tend to be low and high dose peritoneal dialysis as outlined above may be needed or hemodialysis may be preferred. Hemodialysis may especially be preferred by patients with body surface areas exceeding two square meters because a very high dose of peritoneal dialysis would become undully demanding.

Baseline peritoneal equilibration tests are very helpful in diagnosing problems. The development of edema can mistakenly be attributed to changes in peritoneal membrane transport and losses of ultrafiltration if good baseline measurements are not available. Very commonly it is loss of residual renal function which causes the problems in a high

transporter; without baseline studies to reveal that net ultrafiltration has always been quite low, the onset of edema may be misinterpreted. Similarly, low transporters exhibit rising serum creatinine concentrations as the residual renal function declines and this also may be incorrectly attributed to changes in peritoneal membrane transport if good baseline measurements are not available. In low transport patients, the initial low peritoneal dialysis clearances may not be reflected by a high serum creatinine if the residual renal creatinine clearance is substantial. The low peritoneal transport characteristics become apparent as renal function declines and serum creatinine concentration rises; the serum creatinine changes can be misinterpreted by the unsophisticated observer. Rising serum creatinine concentrations in patients with a stable peritoneal equilibration tests and stable residual renal function often indicate non-compliance with dialysis.

Similarly, the development of edema in patients with stable peritoneal equilibration tests and stable residual renal function suggest likely increases in sodium and water intake.

In our experience, peritoneal equilibration tests have changed very little over many years in most patients. Such can occur with frequent peritonitis, followed by loculations with adhesions, and, of course, during acute peritonitis. It is our impression, however, that rising serum creatinine concentrations and/or the development of edema have often been attributed to changes in peritoneal transport when such had not occurred.

An abdominal leak into surrounding tissues, enhanced lymphatic reabsorption, or malposition of the catheter with omental wrapping can result in decreased drainage volumes. If the abdominal cavity can be drained dry prior to a peritoneal equilibration test, the results of the tests are minimally effected by these problems. These problems must be excluded in patients where the peritoneal equilibration tests results are stable and low drainage volumes have developed.

For more detailed information on utilization of the peritoneal equilibration test for planning a peritoneal dialysis prescription and for diagnosing peritoneal problems, several extensive publications are now available [2-4].

For some low transporters, it becomes very demanding in terms of total hours to maintain them on NIPD. CAPD with larger volumes or more frequent exchanges than usual may be more acceptable. Alternatively, for patients who are determined to pursue NIPD, tidal peritoneal dialysis (TPD) may increase small solute clearances enough so that nightly treatments can be reduced by one hour or more [4]. TPD utilizes frequent exchanges on top of an intraperitoneal reservoir. Complete drainage is not attempted until the treatment session is ended. Clearances are probably higher because better fluid membrane contact is maintained throughout the treatment session. During NIPD where with every exchange complete drainage is attempted, there are portions of the cycle time where fluid-membrane contact is minimal and dialysis time is wasted. With TPD, it is important that the tidal volumes be large enough to assure adequate mixing. In our center we often find the best results using reserve volumes ranging from 1500 to 2000 ml and tidal fill volumes ranging from 900 to 1500 ml. The combinations providing the best results may vary from patient to patient. In low-transporters with 8-hours creatinine clearances of only 4 liters on NIPD utilizing 28 liters, we have been able to increase the creatinine clearance over the same eight hours with TPD using the same dialysis solution volume to 4.5 liters. Results in high transporters are more dramatic increasing from 6.5 to 8.2 liters. Obviously the low transporters will need more than eight hours of TPD to achieve their minimum of six liters per day but not as much time as necessary on NIPD. These same low transporters achieved only 5.5 liters per day of creatinine clearance on standard CAPD when residual renal function disappeared and they needed some increase in exchange volume or frequency to reach six liters per day of creatinine clearance on CAPD.

In summary, arbitrarily setting a goal of 40 to 50 liters per week of total creatinine clearance requires tailoring of the peritoneal dialysis recipe based on peritoneal transport characteristics and residual renal function. Measurements of residual renal creatinine clearance and the peritoneal equilibration test are very helpful in guiding the therapy.

Understanding Peritoneal Dialysis Adequacy via Urea Kinetics

The fact that CAPD appears to provide comparable clinical control of uremia to standard hemodialysis is somewhat surprising when viewed from the standpoint of urea kinetics. A recent editorial has dealt with this paradox. Assume that a 70 kg patient ingests enought protein to generate 56 grams of urea nitrogen for removal per week [5]. On peritoneal dialysis, protein intake might need to be increased slightly to account for dialysate protein losses in order to still yield the same 56 grams of urea nitrogen for removal per week. Assume this is the case. If such a patient were receiving hemodialysis monday, wednesday and friday for three hour sessions at urea clearances of 233 ml/minute, then the clearance of urea per treatment session (kt) divided by the distribution space of urea (v which we assume equals 42 liters) would yield a kt/v of 3.0 per week or 1.0 per treatment. This has become rather standard practice. Expected pre and post dialysis serum urea nitrogen concentrations are summarized in

table III. On CAPD, such a patient would be predicted to have a weekly kt/v of 1.7. Note that the time averaged serum urea nitrogen concentration (BUN) on CAPD is above that on standard hemodialysis. Note that the peak BUN values on standard hemodialysis do not exceed the steady BUN level on CAPD. If this patient were placed on hemodialysis with lower clearances (130 ml/minute), the kt/v per week would be near 1.7, the same as for CAPD. The time averaged BUN on low clearance hemodialysis is the same as with CAPD. In contrast the pre-dialysis concentrations on low-clearance hemodialysis all exceed the steady state BUN with CAPD.

Nephrologists might disagree as to whether the patient on standard hemodialysis or the patient on standard CAPD has better control of uremic symptoms. On the other hand, most would agree that the patient on low clearance hemodialysis with pre-dialysis BUN values in the range indicated would be more likely to have umeric symptoms even though this patient has the same time averaged BUN as on CAPD. The National Cooperative Dialysis Study would predict that the low-clearance hemodialysis situation would be more likely to be associated with uremic symptoms[6]. This paradox has led some nephrologists to hypothesize that uremic symptoms may relate to peak concentrations of the BUN and that the amount of time at BUN concentrations above the time averaged concentration may be important relative to the production of uremic symptoms in patients treated by an intermittent therapy such as hemodialysis. If peak control is indeed important, then an intermittent therapy is predestined to require higher clearances than a continuous therapy in order to maintain the peak concentrations at or below the time averaged steady concentrations of the continuous therapy. Hemodialysis with the kt/v of 3.0 per week is required to do just that to maintain the BUN values at all times below the steady state values of CAPD.

The peak concentration hypothesis is an unproven explanation of the kt/v paradox. There are other possible explanations. Perhaps lower clearances of small solutes are better tolerated when combined with high clearances of large solutes as is the case with peritoneal dialysis. Perhaps small solute clearances are not good indicators of uremic control in continuous therapies or in peritoneal dialysis therapies. Most now feel that uremia is a multifactorial syndrome and not caused by a single retained toxic substance.

Maybe intermittent therapies are catabolic due to alternate fluid overload and dehydration and require higher average clearances. Perhaps an analysis of the control of a whole spectrum of molecules is necessary to really compare dialysis treatments relative to control of uremia. Nevertheless, the peak concentration hypothesis should provide stimulation for discussions and further investigations to understand the paradox of the comparable results of CAPD and standard hemodialysis in the face of major differences in weekly urea clearances.

In the meantime it is difficult to utilize standard kt/v recommendations for hemodialysis to formulate appropriate peritoneal dialysis prescriptions. This is not to say that urea kinetic modeling cannot be used to interpret CAPD therapy. However, different kt/v guidelines may need to be developed based on careful prospective studies to analyze clinical outcomes in CAPD patients at different levels of kt/v. If it should turn out to be the case that the maintenance of BUN less than 100 is critical, then this can be done at a much lower kt/v with CAPD than with any intermittent therapy. I would not recommend reducing the weekly kt/v with CAPD much below 1.7 without careful prospective studies. This requires an equilibrated drainage volume (d/p urea = 1) of 10 liters per day in patients in average size adults with no residual renal function. In high to average transporters, this also yields the creatinine clearance of 40 to 50 liters per week.

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