Clinical Grand Rounds

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The Case

51M with a PMHx of ESRD secondary to DM on peritoneal dialysis, type 1 DM, CAD s/p CABG, HFrEF s/p ICD, HTN presents with substernal chest pain. He states that the chest pain lasted for ~10 minutes and was associated with shortness of breath. States he felt anxious prior to his symptoms.

He was arrested 1 day prior to admission. He had not received dialysis since that time.

PD history: was initiated on peritoneal dialysis three years ago. Follows at Mt. Sinai. Has a Baxter catheter. Fast absorber.

Usual prescription: he uses a cycler and does 5 cycles overnight. He predominantly uses 2.5% dextrose solutions with an icodextrin daytime dwell. He infuses 2200 mL. Stated dry weight is 109 kilograms. He has never had peritonitis. He wife assists him with his PD
Medications
- Lantus 40 units at night
- Humalog 30 units premeal
- aranesp 100 mcg qweek
- Ferrous sulfate 325 mg daily
- Vitamin D 2k IU daily
- Calcitriol 0.25 mcg daily
- Calcium acetate 2 tabs TID
- Irbesartan 300 mg daily
- Lasix 160 mg BID
- Colace at bedtime
- Aspirin 81 mg daily

- Plavix 75mg daily
- Simvastatin 20 mg daily
- Synthroid 100 mcg daily
- Prilosex BID

Allergies-none
Past surgical hx-CABG, ICD, PD catheter
Family hx-DM, HTN
Social hx-deny etoh, tobacco, illicit drug use.
Vitals     98.6    HR 60   BP 128/67   pulse ox 95% on RA

Physical exam:
  ◦ General- nad, aaox3
  ◦ Neck- broad neck
  ◦ Chest- no crackles or wheezing. Bilateral breath sounds. Midline sternotomy scar-well healed
  ◦ Cardiac- RRR, s1 s2, no murmurs, rubs
  ◦ Abdomen- PD catheter with no evidence of discharge/erythema at insertion site, clean/dry/intact.
  ◦ Extremities- no edema
Labs
- WBC 12.7
- Hgb/Hct 10.8/33.5
- Plt 374
- Na 128
- K 4.9
- Cl 85
- BUN 75
- Creat 14.3
- Glucose 41
- Trop 0.316-then trended down

Imaging
- Chest xray- PA and lateral
  - Mild pulmonary vascular congestion. No consolidation or pleural effusion
  - ICD and median sternotomy wires

EKG
- Sinus rhythm
- Anterolateral infarct, age indeterminate
The logistics of PD at Bellevue

The hospital uses Baxter and River Renal uses Fresenius.

The ICU level nurses are trained in PD.

1 HD nurse is trained to use the PD cycler.

The general floors do not allow cyclers.

The patient had never done his own PD.

He is on the prison floor, which means anywhere he goes he must have a two officer escort.

On top of all that, he is also trying to get enough phone time so that he can communicate with his lawyer and family about.
Hospital course

Our patient was ruled out for ACS. Due to the lack of PD resources at Riker’s he remained in the hospital.

Once we saw that he would likely stay in the hospital for an extended period of time we ordered icodextrin—it arrived almost two weeks later.

During the first two weeks of his stay, he got an average of 1 liter of UF per day. He would get an average of 8 hours of dialysis with an average of 4 dwells per day. Due to the lack of availability of icodextrin, he did not get an overnight dwell.

To compensate for the reduced amount of PD, his dwell volume was increased and we began to alternate his dextrose solutions on the second week (2.5% and 4.25%).
Course continued

On Hospital Day 15

- An RRT was called for chest pain and he was transferred to MICU for closer monitoring. Placed on an insulin drip for hyperglycemia, anion gap of 22 (his baseline is closer to 15-16). PD was started around the clock. Goal of 8 dwells a day. UF ranged from 1-2 liters daily. There were issues with central supply.
- Course complicated by peritonitis.

On Hospital Day 22

- Another RRT for chest pain and SOB. He was found to have a troponin of 2.5 and so was transferred to the CCU. His troponin peaked at 3.0
- Cardiac cath revealed patent grafts. There was evidence of distal disease but no intervention was performed.
Bun and Creatinine trend
GFR trend
Outline

- Factors involved in PD adequacy
- How to assess peritoneal membrane function
- Dextrose PD solutions compared to alternative osmotic agents
What factors effect PD adequacy?

- Kt/V of urea or creatinine
- Total solute clearance (dialysis plus residual renal function)
- Residual renal function
- Volume status
Kt/V- peritoneal and renal

Kt/V  (daily peritoneal urea clearance /volume of distribution)
- Kt=the ratio of urea in the dialysate compared to the plasma (D/P urea) x the total peritoneal drain volume in 24 hours x 7 days
- V= weight x 60% water volume

The same equation can be used for renal Kt/V, just substitute D/P urea with U/P urea.
ADEMEX

Prospective, randomized control trial.

965 patients were randomized to evaluate whether achieving a peritoneal creatinine clearance (pCrCl) of 60 L/wk per 1.73m² made a difference in the primary endpoint, which was death. They followed the patients for 2 years. There was no statistically significant in the relative risk of death.

Lo et al. performed a randomized prospective study of 320 CAPD patients. They were randomized into three Kt/V targets (1.5-1.7, 1.7-2.0 and >2.0). The end points were survival and clinical outcome. There was no mortality benefit among the groups. The 1.5-1.7 group had more issues with anemia.

A prospective, multi-center, cohort study that evaluated the relationship between PD adequacy and mortality/morbidity.

- The data showed that an increase in the weekly Kt/V of 0.1 was associated with a 5% decrease in relative risk of death.

A re-analysis demonstrated that:

- For each 5 L/wk per 1.73 m² increase in residual GFR (rGFR), there was a 12% decrease in the relative risk of death.
- A 250-ml per day increment in urine volume, there was a 36% decrease in the RR of death.
Residual Renal Function

Prospective multicenter study in the Netherland.

- 413 patients
- They found that for each mL/min/1.73 m2 increase in rGFR, a 12% reduction in mortality rate was found (relative risk of death [RR] = 0.88, P = 0.039). In contrast, no significant effect of pCrCl on patient survival was established (RR = 0.91, P = 0.47).

Prospective single center study

- 246 CAPD patients were followed for ~30 months.
- It showed that patients who had residual kidney function (GFR >/=1) v. anuric patients had improved survival (P=0.005). But anuric patients were sicker (nutritional status, cardiac hypertrophy, anemia, on dialysis longer).
- Wang et al., nephrol Dial Transpland. 2005 Feb; 20(2):396-403
Volume status

Ates et al. did a prospective observational study

- 125 PD patients were followed for 3 years.
- They studied the effect of fluid and sodium removal on the mortality of PD patients

They found that both total and cardiovascular hospitalizations were higher (P<0.001 and P<0.01 respectively) for patients who had a total sodium removal below the median value.

Hypertension (defined as SBP>140 or DBP>90 or 2+ medications) was found to correlate negatively with total volume removal, total sodium removal, Kt/V urea, total hospitalizations and CV hospitalizations

Total Sodium Removal

Three-year patient survival rates in peritoneal dialysis (PD) patients according to the total sodium removal.

The four groups are defined as:

- group I, <130 mmol/24 h/1.73 m²;
- group II, 130 to 181 mmol/24 h/1.73 m²;
- group III, 181 to 232 mmol/24 h/1.73 m²;
- group IV, >232 mmol/24 h/1.73 m².

The three-year patient survival rates were significantly different among these groups (group I, 59.3%; group II, 73.1%; group III, 88.9%; and group IV, 96.1%, $P < 0.01$.)
Total Fluid removal

Three-year patient survival rates in PD patients according to total fluid removal.

The four groups are defined as:

- group I, <1265 mL/24 h/1.73 m²;
- group II, 1265 to 1570 mL/24 h/1.73 m²;
- group III, 1570 to 2035 mL/24 h/1.73 m²;
- group IV, > 2035 mL/24 h/1.73 m².

The three-year patient survival rates were different among these groups (group I, 61.5%; group II, 71.4%; group III, 88.0%; and group IV, 96.3%, $P < 0.01$)
How can we measure solute clearance?

The peritoneal equilibration test (PET) is used to evaluate the transport capabilities of the peritoneal membrane.

The patient instills 2 liters of 2.5% dextrose. At the 4 hour mark, the fluid is drained. Net UF is measured and the fluid is send for measurement of creatinine and dextrose.

Patients are categorized into fast, high average, low average and slow.
Twardowski Curves: Transport Status Based on the Peritoneal Equilibration Test (PET)

Transporters:
Fast- have a high D/P creatinine ratio (>0.8) which means they achieve rapid equilibration of small solutes. But it also means they absorb dextrose faster and as a result lose the osmotic gradient necessary to achieve UF.

High/low average-in between

Slow-have a low D/P creatinine ratio (<0.55), they have a slow rate of equilibration of small solutes and dextrose so they can achieve high UF.

Figure 1: (Left) dialysate creatinine versus plasma creatinine at 4-hours (D/P creatinine); (Right) ratio of dialysate glucose at 4-hours versus dialysate glucose at time zero (D/D₀);
Icodextrin

Icodextrin is a colloid osmotic agent.

Its MW is about 16k Daltons

It gets absorbed via the lymphatic system.


Pharmacokinetics of icodextrin in peritoneal dialysis patients. Moberly et al.

\[\text{Graph adapted from the combination of the following publications:}\]
Icodextrin

Multicenter, randomized, double-blind trial of 92 patients.

PD patients with 4-hr D/P creatinine >0.70 and D/D(0) glucose <0.34. (high-average and high transporters).

They monitored patients weekly for 2 weeks. The control group used 4.25% dextrose for their long dwell.

During the study, the icodextrin group had a significant rise in mean net UF (P<0.001). They had a lower rate of negative net UF (P<0.0001).

A maculopapular rash was reported more significantly in the icodextrin group.

Qi et al. published a meta-analysis of 9 RCTs.

Perit Dial Int March–April 2011 vol. 31 no. 2 179–188
Comparison of the Effects of Icodextrin and Glucose on Net Ultrafiltration During the Long Dwell

<table>
<thead>
<tr>
<th>Outcome analyzed</th>
<th>Studies (n)</th>
<th>Patients (n)</th>
<th>WMD</th>
<th>Results 95% CI</th>
<th>Heterogeneity (p value(^a))</th>
<th>Overall effect (p value(^b))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Different concentration glucose solutions</td>
<td>6</td>
<td>698</td>
<td>287.08</td>
<td>241.28–332.88</td>
<td>0.03</td>
<td>0.00</td>
</tr>
<tr>
<td>1.5% glucose</td>
<td>1</td>
<td>105</td>
<td>460.00</td>
<td>332.38–587.62</td>
<td>NA</td>
<td>0.00</td>
</tr>
<tr>
<td>2.5% glucose</td>
<td>4</td>
<td>428</td>
<td>268.26</td>
<td>215.74–320.78</td>
<td>0.35</td>
<td>0.00</td>
</tr>
<tr>
<td>4.25% glucose</td>
<td>2</td>
<td>165</td>
<td>215.16</td>
<td>77.49–352.83</td>
<td>0.16</td>
<td>0.00</td>
</tr>
<tr>
<td>Different PET categories</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High/high average</td>
<td>4</td>
<td>212</td>
<td>339.60</td>
<td>224.14–455.07</td>
<td>0.39</td>
<td>0.00</td>
</tr>
<tr>
<td>Low average</td>
<td>2</td>
<td>151</td>
<td>146.79</td>
<td>70.18–223.40</td>
<td>0.42</td>
<td>0.00</td>
</tr>
<tr>
<td>Low</td>
<td>2</td>
<td>91</td>
<td>50.96</td>
<td>−50.54, 152.45</td>
<td>0.14</td>
<td>0.33</td>
</tr>
</tbody>
</table>

PET = peritoneal equilibration test; WMD = weighted mean difference; CI = confidence interval; NA = not available.

\(^a\) \(p < 0.05\) indicates the presence of significant heterogeneity across trials. The analysis of heterogeneity is applicable only where more than 1 trial provided data on the relevant outcome.

\(^b\) \(p < 0.05\) indicates the presence of significant overall effect.
Comparison of the effects of icodextrin and glucose on residual renal function.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Icodextrin</th>
<th>Glucose</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>SD</td>
<td>Total</td>
<td>Mean</td>
</tr>
<tr>
<td>Posthuma 2000</td>
<td>2.5</td>
<td>3.12</td>
<td>12</td>
</tr>
<tr>
<td>Wolfson(52w) 2002</td>
<td>2.91</td>
<td>3.74</td>
<td>175</td>
</tr>
<tr>
<td>Plum 2002</td>
<td>2.9</td>
<td>3.58</td>
<td>20</td>
</tr>
<tr>
<td>Konings 2003</td>
<td>3.4</td>
<td>13.08</td>
<td>19</td>
</tr>
</tbody>
</table>

Total (95% CI) | 226 | 157 | 100.0% | 0.07 [-1.10, 1.25] |

Heterogeneity: Chi² = 4.57, df = 3 (P = 0.21); I² = 34%
Test for overall effect: Z = 0.12 (P = 0.90)
Comparison of the effects of icodextrin and glucose on the peritoneal clearances of creatinine and urea nitrogen.

### 4.1.1 Peritoneal clearance rate of creatinine

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Icodextrin Mean</th>
<th>SD</th>
<th>Total</th>
<th>Glucose Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>IV, Fixed, 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posthuma 2000</td>
<td>4.4 0.63</td>
<td>10</td>
<td>10</td>
<td>4.3 0.99</td>
<td>11</td>
<td>10</td>
<td>5.2%</td>
<td>0.10 [-0.60, 0.80]</td>
<td>2000</td>
</tr>
<tr>
<td>Plum 2002</td>
<td>4.03 0.94</td>
<td>90</td>
<td>90</td>
<td>3.47 0.89</td>
<td>85</td>
<td>85</td>
<td>35.3%</td>
<td>0.56 [0.29, 0.83]</td>
<td>2002</td>
</tr>
<tr>
<td>Wolfson(4w) 2002</td>
<td>2.59 0.4</td>
<td>20</td>
<td>20</td>
<td>2.16 0.48</td>
<td>19</td>
<td>19</td>
<td>33.5%</td>
<td>0.43 [0.15, 0.71]</td>
<td>2002</td>
</tr>
<tr>
<td>Finkelstein 2005</td>
<td>3.23 0.82</td>
<td>47</td>
<td>47</td>
<td>2.61 0.74</td>
<td>45</td>
<td>45</td>
<td>25.5%</td>
<td>0.62 [0.30, 0.94]</td>
<td>2005</td>
</tr>
<tr>
<td>Lin 2009</td>
<td>3.53 7.62</td>
<td>98</td>
<td>98</td>
<td>3.16 8.83</td>
<td>103</td>
<td>103</td>
<td>0.5%</td>
<td>0.37 [-1.91, 2.65]</td>
<td>2009</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>265</td>
<td>263</td>
<td>263</td>
<td>100.0%</td>
<td>0.51</td>
<td>0.35</td>
<td>0.67</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi^2 = 2.22$, df = 4 ($P = 0.69$); $I^2 = 0$
Test for overall effect: $Z = 6.17$ ($P < 0.00001$)

### 4.1.2 Peritoneal clearance rate of urea

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Icodextrin Mean</th>
<th>SD</th>
<th>Total</th>
<th>Glucose Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>IV, Fixed, 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wolfson(4w) 2002</td>
<td>4.53 0.96</td>
<td>90</td>
<td>90</td>
<td>4.11 1.01</td>
<td>86</td>
<td>86</td>
<td>35.9%</td>
<td>0.42 [0.13, 0.71]</td>
<td>2002</td>
</tr>
<tr>
<td>Plum 2002</td>
<td>2.67 0.4</td>
<td>20</td>
<td>20</td>
<td>2.28 0.52</td>
<td>19</td>
<td>19</td>
<td>35.7%</td>
<td>0.39 [0.10, 0.68]</td>
<td>2002</td>
</tr>
<tr>
<td>Finkelstein 2005</td>
<td>3.16 0.82</td>
<td>47</td>
<td>47</td>
<td>2.66 0.8</td>
<td>45</td>
<td>45</td>
<td>27.8%</td>
<td>0.50 [0.17, 0.83]</td>
<td>2005</td>
</tr>
<tr>
<td>Lin 2009</td>
<td>3.82 8.12</td>
<td>98</td>
<td>98</td>
<td>3.47 7.1</td>
<td>103</td>
<td>103</td>
<td>0.7%</td>
<td>0.35 [-1.76, 2.46]</td>
<td>2009</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>255</td>
<td>253</td>
<td>253</td>
<td>100.0%</td>
<td>0.43</td>
<td>0.26</td>
<td>0.61</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi^2 = 0.25$, df = 3 ($P = 0.97$); $I^2 = 0$
Test for overall effect: $Z = 4.84$ ($P < 0.00001$)
In conclusion

• Kt/V is not a good way to assess PD adequacy
• Residual renal function is a good prognostic factor in PD
• Volume status correlates well with total and cardiovascular hospitalizations
• Blood pressure control has a significant mortality benefit
• Icodextrin is a good alternative to high dextrose solutions such as 4.25% in fast transporters
Thanks!