Update in Peritoneal Dialysis

Was ist neu?

Berliner Dialyse Seminar

December 8, 2012

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University Health Network
Toronto, Canada
Outline – What’s New?

- PD for heart failure
- Biocompatible PD solutions
- Survival comparisons
Rationale for PD for Heart Failure

- continuous therapy, or at least daily therapy
- better tolerated than HD in the hypotensive patient
- no extracorporeal circuit to fill up
- slow, gentle ultrafiltration
- no myocardial stunning
Myocardial Stunning in HD

demand-associated transient myocardial ischemia during hemodialysis
may be asymptomatic
repeated episodes are postulated to lead to fixed cardiac structural and functional abnormalities, including systolic dysfunction and heart failure

McIntyre. Blood Purif 2010
Why Does Cardiac Mortality in HD Peak 3X week?

- events that were higher after the long interval:
  - all-cause mortality
  - cardiac mortality
  - mortality from infection
  - mortality from MI

PD is Not Associated with Myocardial Stunning

HD #1 Selby Clin J Am Soc Nephrol 2006
HD #2 Selby Am J Kidney Dis 2006
PD Selby Perit Dial Int 2011
Other Advantages of PD for Cardiorenal Syndromes

- no need for arteriovenous access
  - high flow fistulas can increase cardiac work and exacerbate heart failure
- dextrose-based solutions ultrafilter more water than sodium
  - correction of hyponatremia
- very low risk of bacteremia compared to HD
  - important if there is a pacemaker or assist device in place
  *(Thomas et al Perit Dial Int 2012)*
Good Ultrafiltration with PD

- typical UF with a 4.25% dextrose solution is 1000 ml over 4 hours
  = 250 ml/hour
Icodextrin Produces Slow and Steady Ultrafiltration Over the Long Dwell

Net UF (ml)

Time (hr)

Icodextrin

Ho-Dac-Pannekeet et al, Kid Int 1996; 50:979-86
Douma et al, Kid Int 1998; 53:1014-21
Disadvantages of PD

may be harder to get a PD catheter inserted than a venous catheter

- availability of OR time
- surgical expertise
- less of a problem for radiologic or bedside insertions
Disadvantages of PD

- the catheter may not work
- it may stop working
  - constipation, constipation, constipation
- it may leak
- in chronic CardioRenal Syndrome, patient or caregiver has to be taught the technique
- ultrafiltration is not predictable and may vary over time
- risk of peritonitis
PD for CHF: Recent Studies

- mean daily peritoneal UF 670 +/- 225 ml
- GFR did not change over the study (mean F/U 15 months)
- peritonitis very uncommon

Sanchez et al Neph Dial Transpl 2010
Change in Functional Status Before and During PD

NYHA Functional Class

- 3 patients died of heart failure at 5, 12 and 16 months
- improved quality of life
- cost-effective

Sanchez Neph Dial Transpl 2010
More Recent Studies (continued)

Prospective study on clinical effects of renal replacement therapy in treatment-resistant congestive heart failure

Trijntje T. Cnossen¹, Jeroen P. Kooman¹, Harmen P. Krepel², Constantijn J.A.M. Konings³, Nicole H.M.K. Uszko-Lencer⁴, Karel M.L. Leunissen¹ and Frank M. van der Sande¹

• 23 patients with chronic cardio-renal syndrome
• 12 placed on PD, 11 onto HD
• mean GFR 15 ml/min
• mean survival about 16 months, no difference PD vs HD
More Recent Studies (continued)

BUT there was a significant reduction in hospitalizations for CV events when on dialysis, but no difference in total hospitalization.

- no change in left ventricular ejection fraction over time
- improvement in quality of life

Cnossen et al 2012
Survival Comparisons: Still Not Great

Median survival 16 months
- Cnossen Neph Dial Transpl 2012

Mean survival 17.3 months
- Elhalel-Dranitzki Neph Dial Transpl 1998

Mean survival 12.7 months
- Ryckelynck Adv Perit Dialy 1997
Does PD Improve Cardiorenal Syndrome Survival in the Modern Era?

- 28 patients placed on PD for CRS and 34 controls
- 16 month follow-up
- using PD associated with decreased risk of death (HR 0.40), readmission for heart failure
- no improvement in left ventricular ejection fraction in the PD group

Nunez et al Rev Esp Cardiol 2012
Outline – What’s New?

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Local Effects of Glucose on the Peritoneal Membrane

Chronic PD is associated with changes in the peritoneal membrane:

- loss of the mesothelial cells
- thickening of the submesothelial compact zone
- vascular changes
- epithelial-to-mesenchymal transition

Morphological Changes in the Peritoneal Membrane

Normal peritoneal membrane

peritoneum >5 years PD

(Williams et al. Cardiff Peritoneal Biopsy Registry)
How Do We Know that These Changes are the Result of Glucose?

- we don’t
- even hemodialysis and CKD patients have abnormal peritoneal membranes

**BUT**

- animal models show similar changes when the membrane is exposed to hypertonic glucose
- *in vitro*, glucose inhibits mesothelial cell proliferation and causes intracellular damage
Residual Kidney Function (RKF)

Hypothesis

- absorption of GDPs from standard dialysis fluid leads to progressive renal damage
- low-GDP solutions will better preserve RKF
Residual Kidney Function (RKF)

- Some studies have shown better preserved GFR with biocompatible solutions.
- Confounded by decreased peritoneal UF.
How Biocompatible Solutions Could Increase Residual Kidney Function

Less Ultrafiltration
Euro Balance: Improved Urine Volume with Low GDP Solution

Urine Volume
ml/day

std-BAL
BAL-std

Kidney Int 2004 66: 408-18
But: Less Ultrafiltration with “Biocompatible” Solutions

![Bar Graph](image)

- **UF (ml/day)**
- **std-BAL**
- **BAL-std**
- **12 weeks**
- **24 weeks**

- Faster transporter
- Slower transporter
However, Decreased Peritonitis with Biocompatible Solutions?

- neutral-pH, low GDP solutions could be better for peritoneal defense against bacteria
- *if* the new solutions reduce peritonitis, this could be helpful for long-term membrane function
# Does Use of “Biocompatible Fluids” lower Peritonitis Rates?

<table>
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<tr>
<th>YES</th>
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<tr>
<td>Ahmad et al KI Suppl 2006</td>
<td>Lee HY et al Perit Dial Int 2005</td>
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<td>Haag-Weber et al Neph Dial Transpl 2010</td>
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balANZ: Longer Time to First Peritonitis with “Biocompatible” Solution

the group receiving biocompatible dialysis fluid also had a reduction in non-PD infections

Why?

Outline – What’s New?

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Survival Statistics for PD vs HD

- a particular obsession in the United States
- no large randomized controlled trials
- most registry data suggests early survival advantage for PD, late survival advantage for HD
- doctors are taking their patients off PD after 1-2 years because of this!
Selection Bias Explains Apparent Differential Mortality between Dialysis Modalities

Robert R. Quinn,*† Janet E. Hux,‡§¶ Matthew J. Oliver,§¶‖ Peter C. Austin,‡¶⁺⁺ Marcello Tonelli,+++ and Andreas Laupacis§ §§
PD Compared to Planned Start HD

1998-2006
data base in Ontario, Canada
6573 patients started dialysis electively, with > 4 months of predialysis care
  ▪ 2035 patients to PD
  ▪ 4538 patients to HD
mean age early 60’s
50% diabetic
no early survival advantage for PD

*bei gleichen Voraussetzungen*

no change over time to a late survival disadvantage for PD, even in diabetics

suggests that a “time limit” for PD with elective change to HD is not necessary

Why No Late Survival Disadvantage for PD?

OTHER STUDIES

“Early survival benefit for PD”
PD vs all HD
Sick, urgent-start HD patients dying off

“Late survival benefit for HD”

PD vs planned start HD
No early PD survival advantage
Patients dying at the same rate

THIS STUDY

No late survival benefit for HD
Only survivors of HD still alive
Hemodialysis Vascular Access Modifies the Association between Dialysis Modality and Survival

Jeffrey Perl,*† Ron Wald,*† Philip McFarlane,*† Joanne M. Bargman,†‡ Edward Vonesh,§ Yingbo Na,‖ S. Vanita Jassal,†‡ and Louise Moist¶
A Similar Approach to the Early Survival “Advantage” of PD

could the worse early outcome on HD compared to PD be because of tunnelled venous catheters?

what is the outcome on PD compared to HD patients subdivided into

- those starting with tunnelled venous catheters
- those starting with AV fistulas or AV grafts
Who Started HD With a Catheter?

Compared to those starting PD:

- older
- more likely to be diabetic
- more CAD and PVD
- more likely to be referred late to a nephrologist
- started HD with lower albumin, hemoglobin and GFR
Results: You can guess

- HD patients with a catheter had 2-3 fold mortality compared to PD patients (unadjusted AND adjusted)
- HD patients starting with AVF/AVG had same mortality as PD patients
- over time, HD patients starting with AVF/AVG had better survival than PD patients
Survival PD vs HD/catheter vs HD/AVF

UNADJUSTED

ADJUSTED

HD with a catheter
So, does PD Have Worse Mortality Than “Real” HD?

- the group that starts HD with a fistula is a prepared cohort with good protoplasm
- even a successful fistula alone is a marker of some survival advantage
- adjustments can’t compare with the whole cohort starting PD
So Should Everyone Start Dialysis With a Fistula and HD to Maximize Survival?

- first of all, it’s not all about survival
  - “there’s more to living than not dying”
- the planned start with a fistula reflects the healthiest, most prepared patients
Effect of Clopidogrel on Early Failure of Arteriovenous Fistulas for Hemodialysis
A Randomized Controlled Trial

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<th>Table 3. Fistula Suitability Failure</th>
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<td>No. (%) of Patients</td>
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<td>Suitability failure (all patients)</td>
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<td>By location</td>
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<td>Forearm fistula</td>
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<td>Upper arm fistula</td>
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Dember et al J Am Med Assoc 2008
So Was Ist Neu (I)?

PD is an effective and under-used modality to treat chronic cardiorenal syndrome

- may or may not prolong survival
- good for symptom control and quality of life

Biocompatible PD solutions may be more expensive, but not necessarily better

- “improvement” in residual kidney function likely related to less ultrafiltration
- there may be a reduction in peritonitis
probably much of the survival advantage, especially early on, of PD over hemo has to do with planned start and absence of a hemodialysis catheter

when PD is compared with hemo patients with a planned start and AVF/G, survival is strikingly similar

usually the best modality is the one chosen by a patient educated about their options