Peritoneal Dialysis Adequacy and Complications

Balazs Szamosfalvi, MD
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PD Adequacy

Computer-Aided PD prescription and monitoring (PET test)

- Preservation of residual kidney function
- Biocompatibility of peritoneal dialysate
- Novel techniques must be cost-effective

Adequacy of Dialysis

- Good nutrition, Healthy lifestyle
  Patient involvement
- Automated PD, Wearable Artificial Kidney with sorbent cartridge

OUTCOME:
Quality of life
Rehabilitation
Morbidity & Mortality

Good nutrition,
Healthy lifestyle
Patient involvement

Automated PD, Wearable Artificial Kidney with sorbent cartridge

Novel techniques
must be cost-effective

Quality of life
Rehabilitation
Morbidity & Mortality

PD Adequacy

Computer-Aided PD prescription and monitoring (PET test)
PD Adequacy

1. Brief PD physiology
   - Anatomy of the peritoneum
   - Principles of solute and volume transport in PD
   - Some modalities of PD

2. Small solute transport
   - The PET test
   - Nutrition: protein equivalent of nitrogen appearance (PNA or PCR)
   - Modality selection (CAPD, CCPD, NIPD etc)
   - Studies of clinical outcomes with different weekly Kt/Vurea goals
   - Updated K-DOQI guidelines (2006)
Anatomy of the peritoneum

- Surface area 0.5-2 m²
- Lined with mesothelial cells
- Blood flow ≈ 80 ml/min
- Changes with PD
  - Mesothelial cells (degeneration and hyperactivity)
  - Vascular changes (subendothelial hyalinization) – like DM
  - Collagen deposition

Krediet RT: Peritoneal anatomy and physiology during peritoneal dialysis; in Replacement of Renal Function by Dialysis, 5th edition; p116
3 Pores for Solute and Water Transport

Blood in Peritoneal Capillaries

Small pores 95% (4-6 nm): Urea, creatinine

Large pores 5% (> 20 nm): macromolecules

Aquaporin 1 (1 nm): water transport

Endothelium

Mesothelium

Dialysate filled Peritoneal Cavity

Solute and Water transport in PD

I. Variable diffusive solute transport properties; may change with time for a specific patient
   ▪ High transporter (1 STD above average; worse clinical outcomes)
   ▪ High-average transporter
   ▪ Low-average transporter
   ▪ Low-transporter (1 STD below average)

II. Ultrafiltration/convection
   ▪ Dependent on osmotic and colloid osmotic pressure
   ▪ We cannot generate a negative hydraulic pressure in PD (compare with hemodialysis ultrafiltration)
   ▪ Requires a favorable pressure gradient and functioning pores
   ▪ Daily albumin losses are substantial but well-tolerated

III. Lymphatic reabsorption
   ▪ Patients may have variable rates of reabsorption
The PET Test 1

1. The peritoneal equilibration test (PET) is a semi-quantitative assessment of peritoneal membrane transport function:
   - After a long 10-12 h dwell, 2 liters of a 2.5% dextrose solution is infused for a 4-hour dwell
   - Highly standardized (inflow and drain duration, positions, serum and dialysate sampling, laboratory analysis)

2. Information obtained
   - Dialysate to plasma ratios of solutes at 0, 120, 240 minutes (urea, creatinine, sodium, electrolytes, protein)
   - D(t)/D0 ratios for glucose are obtained from the dialysate
   - Drained volume helps evaluate ultrafiltration

Time-dependent changes during peritoneal dialysis in dialysate (D) concentration of glucose (left panel) or creatinine (right panel) as a proportion of original dialysate glucose concentration (DO) or plasma creatinine concentration (P), respectively. High transporters have excessive glucose absorption and are at risk for ultrafiltration failure and malnutrition due to amino acid losses. Low transporters are at risk of inadequate small solute removal.

1. ©UpToDate; Data from Twardowsky, ZJ, ASAIO Trans 1990; 36:8.
Differences between rapid and slow transporters during PD. Rapid transporters reach creatinine equilibration more quickly (dialysate-to-plasma creatinine equals one, top panel), have a gradual reduction in dialysate volume after two hours due to glucose absorption (middle panel), and have a reduction in creatinine clearance ($C_{cr}$) after four hours due to absorption of creatinine with the glucose and fluid (lower panel). Thus, short dwell times are most efficient in these patients. Values are shown for the major types of PD: nightly intermittent with short dwells (NI); daytime (DA) and continuous ambulatory (CA); and continuous cycling at night (CCN) with short dwells and during the long daytime dwell (CCD).

1. ©UpToDate; Data from Twardowsky, ZJ, ASAIO Trans 1990; 36:8.
Nutritional Assessment

1. Clinical assessment:
   - History, physical examination
   - Laboratory tests (albumin, etc)

2. Normalized protein equivalent of urea nitrogen appearance (nPNA) in PD
   - \( nPNA = 6.25 \times (\text{Urea appearance} + 1.81 + [0.031 \times \text{lean body weight, kg}]) \)
   - Urea appearance, g/day = \((Vu \times Cu) + (Vd \times Cd)\)
   - A target of 1.0-1.2 g/kg per day or higher is recommended

Various PD modalities

- Continuous Ambulatory PD (CAPD)
- Continuous Cycling PD (CCPD)
- High Dose CCPD
- Nocturnal Intermittent PD (NIPD)
- Tidal PD (TPD)

Gokal R: Dialysis techniques: Peritoneal Dialysis; in Replacement of Renal Function by Dialysis, 5th edition; p670
Selecting and adjusting a PD prescription

Assess Patient Parameters

- Patient Size (BSA in m²)
- Clinical Assessment (protein catabolic rate)
- Residual Kidney Fx

Set 1st Month’s Prescription

Delay 4 weeks for PET

Adequacy Assessment

Prescription Adjustment

Nutrition Assessment

Clinical Assessment

Clearance Assessment

No Adjustment

Yes

Targets Achieved

No

Adjust PD with PET

Adapted from Gokal R; in Replacement of Renal Function by Dialysis, 5th edition; p675
PET helps select PD modality

1. ©UpToDate; Misra M and Khanna R: PET Test
The CANUSA Study 1

1. Prospective, cohort, multicenter observational study in Canada and the United States
   • Each 0.1 unit decrease in total (PD and RRF) Kt/Vurea was associated with a 5% increase in the RR of death
   • A Kt/Vurea of 2.1 and a weekly creatinine clearance of 70 L/1.73 m² body surface area were both associated with a 78 percent expected two-year survival rate
   • RRF and PD clearance were assumed equivalent

2. Reanalyzed to determine role of RRF versus PD Kt/V
   • Residual renal clearance then emerged as the most important predictor of mortality

The CANUSA Study 2

The ADEMEX Study

1. Prospective, randomized, trial of different PD doses conducted in Mexico\(^1\)
   - 965 patients assigned to 4 x 2 L PD or an increased prescription to achieve CCr > 60 L/1.72 m\(^2\)
   - Good separation of dose (Kt/Vurea 1.62 versus 2.13 and Ccr 46 versus 57 L/week/1.72 m\(^2\))

2. Outcomes
   - There was no difference in survival between the two groups (68% versus 69%) at study end
   - There was no difference in quality of life
   - Survival was not different even in the subgroups of anuric patients

The Hong Kong PD Study

1. Prospective, randomized, trial of different PD doses conducted in Hong Kong

- 320 new CAPD patients with < 1 renal Kt/V urea were assigned to prescriptions to achieve 1.5-1.7 or 1.7-2 or >2 Kt/V urea
- Dose separation took 1 year to achieve

2. Outcomes

- There was no difference in survival, serum albumin or hospitalization rates
- The lowest Kt/V group had more uremic symptoms and higher erythropoietin requirements


1. Patients with residual kidney function (RKF) (urine volume is >100 mL/day):
   - Minimal delivered total weekly Kt/Vurea (PD+RKF) ≥1.7
   - Total (PD+RKF) solute clearance must be measured after 1 month and every 4 months thereafter
   - 24-hour urine collection for volume and RKF every 2 months

2. Patients without RKF:
   - Minimal delivered weekly Kt/Vurea ≥1.7
   - Total solute clearance must be measured after 1 month and every 4 months thereafter

PD Complications

- Ultrafiltration Failure
- Biocompatibility: Glucose degradation product and icodextrin-related complications
- Encapsulating sclerosing peritonitis
- Peritonitis
- Mechanical and other
The PET used to assess Na-sieving

Sodium D/P (dialysate/plasma) ratios versus time as measured in 1985 (5/23/85, white curve) and 1992 (7/06/92, black curve) in a patient with progressive loss of ultrafiltration. Values are superimposed upon the standard curves. The initial curve is normal, displaying an initial drop of the ratio; the second curve is abnormal with no decrease at the beginning of dwell. The curve rises steadily after a one hour dwell.

1. ©UpToDate; Misra M and Khanna R: Mechanisms of solute clearance and ultrafiltration in peritoneal dialysis; accessed 08/04/2009
PET helps diagnose UF failure (UFF)

UF Failure
- Type 1: >50%
- Type 2: <10%

3. Gomes et al: Categorization of sodium sieving... NDT 2009; 0: gfp319v1-gfp319
# Biocompatibility of PD fluids

## 1. Glucose-related problems[^1]
- Un-physiologic (very high) glucose content induces cellular and interstitial changes (TGF-β, VEGF signaling)
- Toxic glucose degradation products are formed during heat sterilization of single compartment bags

## 2. Icodextrin (hexose oligo-polysaccharid) as colloid osmotic:
- 10-15% absorbed and results in elevated plasma maltose levels: can cause pseudo hyperglycemia by cross-reacting with glucose on some portable glucometers[^2]
- Sterile peritonitis, particularly with some batches with toxic contaminants (bacterial peptido-glycans)[^3]

Structure of Icodextrin

Branch

Branch point
$\alpha$ (1→6) linkage

Main $\alpha$ (1→4) chain
Icodextrin Sterile Peritonitis

1. Etiology and Incidence:
   - 2001 incidence estimated 10-30% per year
   - Manufacturer reports link to batches with peptidoglycan (PGN) concentration >10 ng/ml

2. Recurrent icodextrin sterile peritonitis
   - 7 patients (20%) exposed to recalled lots developed sterile peritonitis
   - 2/7 resolution despite continuing icodextrin; 2/7 undergo catheter removal
   - 3/7 clear when icodextrin stopped, recur with re-exposure to PGN free dialysate
   - Hypersensitivity to trace amounts PGN vs. novel antigen

Toxic glucose degradation products (GDPs) in Peritoneal Dialysis Fluid

Acetaldehyde
Glyoxal
Methylglyoxal
3-deoxyglucosone
Formaldehyde
3,4-dideoxyglucosone-3-ene (3,4-DGE)

Alterations of the peritoneum on PD: Effects of Chronic Glucose Dialysate

Initiation of CAPD

25 months CAPD

Mateijsen M. Perit Dial Int 19:517, 1999)
Sclerosing Encapsulating Peritonitis

1. Etiology and diagnosis (incidence 0.5-2.5% of PD patients):
   - Usually develops after years of PD
   - Associated with high glucose and acetate in PD fluid, prior peritonitis, beta-blockers
   - Diagnosis established with imaging findings (CT or MRI)

2. Treatment:
   - Adjust PD regimen for maximum biocompatibility (early EPS)
   - Transfer patient to HD temporarily or permanently
   - Corticosteroid treatment
   - Expert surgical adhesiolysis

3. Prognosis:
   - Risk of death and PD technique failure with transfer to HD high

Sclerosing Encapsulating Peritonitis
Peritonitis in the PD patient

1. Etiology and diagnosis:
   - Differentiate simple versus complicated (transluminal-touch contamination, peri-luminal, trans-visceral, hematogenous)
   - <1 % associated with bacteremia
   - Evaluate symptoms; fluid cloudiness, WBC count, cultures

2. Prevention is the most important intervention:
   - Proper training of the patient in exchange procedures
   - Use of Y-connect system possible with double bags; APD
   - Antibiotic prophylaxis before bacteremic procedures (e.g. dental, colonoscopy) and PD catheter insertion

3. Treatment (usually with intra-peritoneal antibiotics)
   - Consider severity and local antibiotic sensitivity profile
   - Use non-nephrotoxic drugs to preserve RKF
Y-connection with double bag for CAPD

- Fresh fluid: no need for manual spike
- Drain bag: pre-connected; sterile
- Minimizes risk of intraluminal contamination

## Other PD Complications

1. **Mechanical complications:**
   - Gastroesophageal-reflux and delayed gastric emptying: Reduce fill volume if feasible, use motility agents (metoclopramide, erythromycin)
   - Back and abdominal pain: reduce fill volumes if possible, CCPD, use more bio-compatible fluids
   - Pleural effusion due to pleuro-peritoneal leak: 1.6-10% of patients; reducing supine fill volumes and pleurodesis may help

2. **Other complications**
   - Hypokalemia: more liberal K diet and or supplements will usually correct the problem
   - Hypomagnessemia: theoretically a 0.5 mmol/L PD Mg level may be optimal; hypermagnessemia should be avoided as it may contribute to adynamic bone disease