



Renal Replacement Treatment for End Stage Renal Failure - The Role of CAPD

Vijay Kher*, Alok Kr Gupta**

*Sr. Consultant, ** Registrar, Deptt. of Nephrology, Indraprastha Apollo Hospital, New Delhi

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ABSTRACT

CAPD is one of the three modalities of renal replacement therapy available to patients with end-stage renal disease (ESRD). Role of CAPD has evolved over the past few years and has become an important therapeutic modality for ESRD in our country. Automated peritoneal dialysis in which exchanges are done by a cyclor rather than manually as in CAPD, has also established its role. There has been important modification in the technique of CAPD like Y systems with pre-attached bags, which has significantly reduced peritonitis rates. CAPD has certain definitive advantages like minimal need for infrastructure, domiciliary treatment, simple procedure, no need for vascular access, low requirement of erythropoietin, better tolerance by diabetics, infants and children, low risk of acquiring chronic hepatitis viruses, and improved preservation of residual renal function. Basic principles of CAPD, peritoneal equilibrium test for characterizing transport characteristic of the peritoneal membrane, peritoneal dialysis adequacy and complications of technique will be discussed in this article.

INTRODUCTION

Patients with end-stage renal disease (ESRD) require renal replacement therapy (RRT) for sustaining life and these consist of haemodialysis (HD), peritoneal dialysis (PD) and renal transplantation (RT).

Peritoneal dialysis is in widespread use for the treatment of ESRD, being used by more than 100,000 patients worldwide. PD should not be thought of as a technique in competition with haemodialysis but rather as a complimentary modality and part of range of therapies that can be offered to the ESRD patients. PD should be part of an integrated program of renal replacement therapy that comprises HD, PD and RT.¹ Depending on the circumstances patients could move from one form of RRT to another as shown in Fig. 1.

Moncrief and Popvich first introduced CAPD in 1975² and later this technique was popularized and introduced in an ambulatory form by Oreopoulos in 1977.³ In India there are several impediments to renal replacement therapy and an extremely small percentage of the ESRD population is able to avail of the various RRT options.⁴ Presently there are over 80 centers doing CAPD in India. The penetration of CAPD as a modality of treatment of ESRD in India has increased from 5 % in 1996 to 14 % in 2000. The growth rate is around 30 %, which is the highest amongst all Asian countries.⁵ Approximately 4000 patients have been initiated on CAPD in last 10 years of which 2000 are still continuing on CAPD.⁶

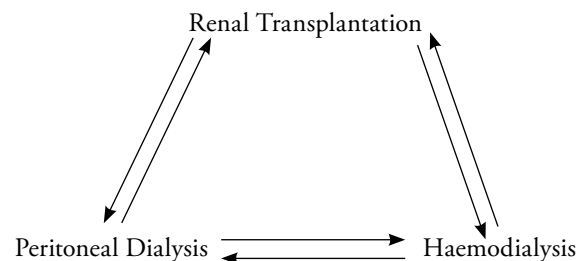


Fig. 1 : Movement of ESRD patients from one form of renal replacement therapy (RRT) to another.

Before discussing clinical application and its complications, it is extremely important to have an understanding of the relevant peritoneal anatomy and physiology. In essence PD involves the transport of solutes and water across a 'membrane' that separates two fluid containing compartments:

1. Blood in peritoneal capillaries, which contains uremic toxins
2. Dialysis solution in the peritoneal cavity, which contains sodium, chloride, lactate and dextrose.

Peritoneal membrane is a heterogeneous, heteroporous, semi-permeable membrane with relatively complex anatomy and physiology.

ANATOMY AND PHYSIOLOGY OF PD

Peritoneal membrane is composed of two layers, parietal peritoneum (about 10 % of total) covering the inner surface of the abdominal wall, and visceral peritoneum (about 90%

of total) covering the visceral organs. Peritoneal cavity is the potential space between these two layers. The total surface area of the peritoneal membrane is approximately equal to body surface area in most adults (i.e. 1 to 2 m²). The peritoneal cavity usually contains about 100 ml of fluid but can usually tolerate 2L or more of fluid without discomfort or compromise of pulmonary function.⁷

Anatomic component important for PD

1. **Mesothelium:** It is a continuous monolayer of cells, secreting surfactant like lubrication for the peritoneum. They modulate host defense and have been shown to produce CA 125. The CA 125 appearance rates in the dialysate effluent may be used to estimate mesothelial cell mass and possibly the effect of changing to more “biocompatible” solutions on overall peritoneal membrane health.
2. **Basement membrane:** It is a homogenous 25-30 nm thick layer underlying mesothelial cells, composed of type II collagen proteoglycans, and glycoproteins.
3. **Interstitial:** It is the supporting structure of the peritoneum composed of muco-polysaccharide matrix and containing collagen fibres, blood vessels, lymphatics, glycosaminoglycans and fibroblasts. The aqueous phase of interstitium mediates transport of water, electrolytes, protein, nutrients and hormones.
4. **Blood vessels:** Total splanchnic blood flow in normal adult humans at rest ranges from 1 to 2.4 L/min and arises from coeliac, superior and inferior mesenteric arteries. Exact blood flow to peritoneum is probably 50-100 ml/min.
5. **Peritoneal lymphatics:** There is a network of lymphatic vessels that aid in removal of fluid and solutes from the interstitium. Intraperitoneal hydrostatic pressure, body posture and pharmacological agents alter the rate of lymphatic uptake.

Peritoneal membrane acts as a “dialyzer”. There are six layers contributing to resistance.

1. Stagnant capillary fluid film overlying the endothelium of the peritoneal capillaries.
2. Capillary endothelium
3. Endothelial basement membrane
4. Interstitium
5. Mesothelium
6. Stagnant fluid film overlying the peritoneal membrane.

Newer concepts, such as three pore model for peritoneal transport have emerged and suggest that peritoneal capillary endothelium and its basement membrane offers the major resistance to peritoneal transport. Also colloid-rich, water-poor phase of interstitium offers significant resistance to solute transport. The three pore model suggests that the peritoneal capillary is the critical barrier to peritoneal transport, and solute and water transport across it is mediated by pores of different sizes.⁸

1. Large pores with a radius of 20-40 nm - macromolecules like proteins are transported by convection.
2. Small pores with a radius of 4.0 - 6.0 nm - correspond to interendothelial clefts; they are responsible for transport of small solutes such as urea, creatinine, sodium and potassium.

3. Ultra pores with a radius of < 0.8 nm - responsible for water transport and probably correspond to aquaporins.

Physiology of peritoneal transport

Peritoneal transport comprises of diffusion, ultrafiltration and fluid absorption that occur simultaneously.

1. **Diffusion :** Defined, as a tendency of solutes to disperse themselves within the space available and move across dependent on concentration gradient. It is the most important mechanism for solute transport into the peritoneum. Diffusive clearance of any solute in PD depends on the “effective peritoneal” membrane surface area, the intrinsic permeability of the membrane, dialysate flow, concentration gradient, and time allowed for transport.
Typical dialysate flow rate are markedly lower than capillary blood flow or membrane transport capabilities, therefore becoming the limiting factor for standard PD therapies. Diffusion becomes more restricted as molecular weight increases.
2. **Ultrafiltration (UF):** Net ultrafiltration is achieved by creating an osmotic pressure gradient between blood and dialysate. Solute present in body fluids are swept along the bulk solvent flow, which is termed as “solvent drag” or “convection”. Conventionally various concentrations of glucose (dextrose) is used as osmotic agent. It induces transcapillary ultrafiltration across both small interendothelial and ultra small transcellular pores / aquaporins. Polymers of glucose (icodextrin or polyglucose, incorporated in new dialysis fluids) which are not absorbed, induce a colloid osmotic force to drive ultrafiltration across interendothelial pores. Ultrafiltration with glucose is rapid and occurs early in dwell and decreases with time as glucose is absorbed, whereas with polyglucose, ultrafiltration is constant but slow.
3. **Absorption:** Intraperitoneal fluid is continuously absorbed from the peritoneal cavity into the tissues of the abdominal wall from which it is taken up by lymphatics and peritoneal capillaries. A small proportion is absorbed directly into the subdiaphragmatic peritoneal lymphatics. Typical values for peritoneal fluid absorption are 1.0 - 2.0 ml/min of which 0.2 - 0.4 ml/min go directly into the lymphatics.

Peritoneal equilibration test (PET)

Peritoneal transport is assessed clinically with the help of PET described by Twardowski et al.⁹ Equilibration ratios between dialysate and plasma for urea (D/P urea), creatinine (D/P Cr), sodium (D/P Na), and so forth, are used to assess peritoneal transport. These ratios measure combined effect of diffusion and ultrafiltration and are affected by the molecular weight of the solute, membrane permeability and effective surface area. Conventionally, test is performed in the morning after complete drain of the prior long dwell. Using 2.5 % dextrose dialysate, patient’s usual fill volume is infused. A sample of dialysate for determination of creatinine, urea and glucose is taken immediately after infusion and at 2 and 4 hours. Blood sample for determination of creatinine, urea and glucose is taken at 2 hours after infusion. Dialysate is drained after 4 hours and the drain volume is recorded. The dialysate to plasma (D/P)

Table 1 : Composition of CAPD Fluid ²⁴

Component	Concentration (mmol/L)
Sodium	132
Potassium	0-2
Calcium	1.25
Magnesium	0.25
Chloride	95
Lactate	40
Dextrose	1.5, 2.5 or 4.25 %

ratios for creatinine and urea, and the ratio of glucose in the dialysate compared to its initial concentration (D/D_0) at times 2 and 4 hours are calculated and plotted in standard PET graph. Peritoneal membrane transport is divided into four categories: high, high average, low average and low. High transporters have highest D/P ratios and vice versa. High transporters most rapidly equilibrate creatinine (and urea) and achieve excellent solute clearance. However they also rapidly absorb glucose from peritoneal cavity thereby dissipating the osmotic gradient. Therefore, they have low drain volumes and absorb more fluid during long dwells. These patients benefit from CCPD with more frequent exchanges and shorter dwell time. They may also benefit from the use of icodextrin during their long day dwell.¹⁰ On the other hand, patient who exhibits low membrane transport have poorer solute clearance and benefit from longer dwell times and larger exchange volumes. They ultra-filter very well because there is slow dissipation of osmotic gradient. Patients in the two average groups tend to do well with both solute clearance and ultrafiltration.

PERFORMING CAPD - APPARATUS

For performing basic function of repeated delivery of fluid to the peritoneum and to take it out with sterile technique, a permanent catheter in peritoneum, biocompatible dialysis solution and education and training of patient or care provider is required.

Basic system consists of

1. CAPD catheter
2. Catheter connected to transfer set
3. Transfer set linked to infusion set
4. Infusion set spiked into the CAPD bag

Earlier after infusion of fluid the bag was folded and worn on the patient during dwell time and become the drainage bag for the next cycle. To start a new cycle after draining, the set was disconnected and a fresh bag was spiked and infused. This method was cumbersome and had high rates of peritonitis. To overcome these problems, Y set was developed.¹¹ Objective was to free patients from the requirement to remain attached to the transfer set and empty bag between exchanges. This is a Y-shaped tubing with its stem attached to patient's catheter and afferent and efferent limbs attached to a bag of fresh PD solution and to a drain bag respectively. This method also incorporated "flush before fill" principle in which about 100 ml of fresh solution is flushed from the new bag through the afferent limb of the Y. This concept substantially reduced the rates of peritonitis. In a further modification, solution bag and drain bag comes preattached to

the afferent and efferent limb of the Y, so obviating the need for any spike connection. This is called as double bag system.

CAPD Catheters

A permanent and trouble-free access is required for maintaining proper inflow and outflow of PD fluid and preventing catheter tip migration, dialysis fluid leaks and exit site/ tunnel infections.

Tenckhoff and Schechter¹² in 1968 designed first workable catheter. It consisted of silicon rubber catheter with a coiled intraperitoneal segment; a Dacron cuff at the peritoneal exit; a short subcutaneous part in the tunnel; and a second external cuff just before the skin exit site. Coiled intraperitoneal segment was modified to a straight segment. Tenckhoff catheter still remains a common CAPD access catheter. Several new and better catheters have been developed. Swan-neck catheter is an improved device with a lateral or downward external exit and a permanent band in the subcutaneous portion. Silicone rubber is used most frequently as material for PD catheter as it is relatively biocompatible, inert and has non-leachable plasticizers.

CAPD fluid / solutions

Dialysis solutions consist of electrolytes, osmotic agents and buffers. Solutions are composed to effectively remove nitrogenous wastes, excess water, and correct electrolytes and counter acidosis. Composition of CAPD fluid is given in Table 1.

PERITONEAL DIALYSIS – TYPES

CAPD: Commonly patient performs four manual exchanges during day. In addition, patient may do another exchange during night manually or through night exchange device, thus increasing the number of exchanges.

1. Cycler dialysis: In this modality patient uses a cycler machine to perform exchanges instead of doing them manually. In CCPD (continuous cyclic peritoneal dialysis) cycler performs multiple exchanges overnight and delivers a dialysate exchange at the end of the nighttime cycler dialysis. In NIPD (nocturnal intermittent peritoneal dialysis), patients perform cycler dialysis overnight but do not perform the day exchange (dry day).
2. Tidal peritoneal dialysis (TPD): It consists of the repeated instillation of small tidal volumes of dialysis fluids with the use of an automated cycler.

DIALYSIS PRESCRIPTION

At the time of initiating PD, prescription is usually advised empirically. After about a month of initiating of dialysis, 24 hour collections of urine and dialysate along with serum chemistry should be performed in order to calculate weekly Kt/V urea and creatinine clearance. Initial PET should also be performed at 1 month after the initiation of dialysis. PET is performed to document transport characteristic of a particular patient. High and high average transporters require short dwell prescriptions as they have early loss of osmotic gradient. Low transporters usually require high dose CAPD or CCPD in order to maintain adequate dialysis.

For CAPD patients, increasing dwell volume and also increasing number of exchanges /day is helpful. Alternatively a nocturnal exchange during night may be done. For cycler patient, several

Table 2 : Advantages of CAPD

- Freedom from machine
- Performance at home
- Rapid training
- Reduced cardiovascular stress
- Avoidance of heparin
- Use of drugs intraperitoneally like insulin, antibiotics
- Constant blood purification
- No peaks and troughs
- Good middle molecule clearance
- Preserves residual renal function (RRF)
- Need for lesser dose of EPO

Table 3 : Limitations of PD

- Unsuitable abdomens
- Cannot / will not learn
- Body size limits with low transport
- Anuric patients or low residual renal function
- Family fatigue or boredom

methods are available for improving adequacy. These include increasing the time spent overnight on the cyclor, increasing the number of exchanges on the cyclor or increasing the number of daytime dwells. Various combination of above measures can be used in a particular patient to achieve adequate clearance.

ADEQUACY OF PERITONEAL DIALYSIS

The National Kidney Foundation (NKF/DOQI) clinical practice guidelines, last revised in 2000¹³ provide evidence-based guidelines for the provision of adequate PD. Currently weekly Kt/V urea and weekly creatinine clearance for both peritoneum and residual kidney function is calculated and used as markers of adequacy. For CAPD patients, the delivered PD dose for Kt/V urea should be a least 2.0. The recommended weekly creatinine clearance should be 50-60 L/week/1.73 m². APD patients have slightly higher Kt/V target (2.1 for CCPD and 2.2 for NIPD). After the last PD guidelines were revised by NKF / DOQI workgroup, the ADEMEX trial was published.¹⁴ Nine hundred sixty patients were randomized to either the control or intervention group in a 1:1 fashion. In the control group patients continued on their present PD prescription. In the intervention group treatment was modified to achieve a peritoneal creatinine clearance of 60 L/wk/1.73m². Residual renal function was similar in the two groups. The mean separation between the two groups in terms of peritoneal creatinine clearance was approximately 10L/wk/1.73m². Patient survival was found to be similar in both the groups even after adjustment for comorbid conditions such as age, presence of diabetes mellitus, serum albumin levels, anuria and normalized protein equivalent of the nitrogen appearance. The advantages, limitations and contraindications of CAPD are discussed in Table 2, 3 and 4.

COMPLICATIONS OF PERITONEAL DIALYSIS

These can be divided into infectious and non-infectious complications.

Table 4 : Avoid CAPD

- Obese patients, abdominal surgery
- Hernias
- Unhygienic environment
- Obliterated peritoneal space
- No motivation

A. Infection-related complications

These include peritonitis and exit site or tunnel infections and account for two-thirds of all catheter losses.

1. Peritonitis: Most common infection-related complication responsible for hospitalization, catheter loss, malnutrition, peritoneal membrane failure and occasionally death. Average frequency was reduced from 1.1-1.3 episodes per patient-year to 1 every 24 months primarily due to use of Y systems with preattached bags and flush before fill technique.¹⁵ Peritonitis is diagnosed if at least two of the three criteria are present.¹⁶
 - i. Cloudy dialysis effluent with dialysate TLC > 100 cells/μl (> 50 % neutrophils)
 - ii. Abdominal pain
 - iii. Positive culture from dialysate

Majority of infections are bacterial (80-90%) of which skin bacteria, *Staph. epidermidis* and *Staph. aureus* account for > 50 % cases. Fungi and tubercular infections are present in 2-3 % of cases.¹⁷ Culture-negative cases account for 5-20 % of all cases and this proportion is higher in our country. In India the incidence of peritonitis is 1 in 18-20 patient months.⁶

Treatment of peritonitis is based on International Society for Peritoneal Dialysis (ISPD) recommendations.¹⁶ After obtaining dialysate sample for culture, patients are put on a combination of first and third-generation cephalosporins. Aminoglycosides are contraindicated in non-anuric patients and can be given to anuric patients in place of ceftazidime. Treatment has to be modified after culture reports and usual duration of treatment is 2-3 weeks. ISPD does not recommend routine use of vancomycin for fear of inducing vancomycin-resistant enterococcus.¹⁶ Tubercular peritonitis has a higher incidence in endemic areas (upto 3 %). It is diagnosed on the basis of positive AFB culture of dialysate. Usually triple-drug therapy (Rifampicin, INH, Pyrazinamide) for duration of 9-12 months is required.¹⁸ It is a common problem among Indian patients.⁴⁻⁶

Indications of catheter removal include refractory or relapsing peritonitis, fungal and tubercular peritonitis, chronic exit site or tunnel infection, non-responding *Pseudomonas* peritonitis and secondary bacterial peritonitis.

2. Exit site and tunnel infection: Patients present with purulent drainage and local erythema. It contributes significantly to peritonitis and catheter loss. Bacteriology of exit site is very similar of that of peritonitis. After obtaining drainage for culture and Gram stain, patient is given antibiotics as per ISPD guidelines.¹⁶ Catheter may need to be removed in case of treatment failure.

Staph. aureus nasal carriage is associated with increased risk of exit site infections, tunnel infections, and peritonitis.¹⁹ These patients require eradication of nasal carriage by local mupirocin or oral rifampicin and daily exit site care with mupirocin. Some exit site infection extends into the subcutaneous tunnel, which may be evident only on ultrasonography examination of the tunnel tract. Tunnel infections are difficult to eradicate and particularly when associated with peritonitis. These require catheter removal.

B. Non-infection-related complications

I. Metabolic Complications

1. Hypoalbuminemia: Patient performing PD loses approximately 4-7 grams of albumin per day. Patients need to take > 1.2 g/kg/day dietary protein to offset hypoalbuminemia.²⁰
2. Hyperglycemia, hypertriglyceridemia, weight gain: Glucose remains standard osmotic agent for PD. It is easily absorbed across peritoneal membrane and contributes to hyperglycemia, hypertriglyceridemia and weight gain. These patients require low calorie diet, lipid lowering agents and strict adherence to fluid restriction thereby minimizing need for hypertonic dialysate. Use of non-glucose-based dialysate, icodextrin, is an alternative.¹⁰
3. Anemia: Anemia is managed with erythropoietin, iron and multivitamins. EPO requirement is significantly lower as compared to patients receiving hemodialysis.²¹
4. Hypokalemia: Standard dialysis solution has zero potassium. Hypokalemia has been reported in 10-30 % of CAPD patients and are usually associated with poor nutritional intake. Only those patients who are non-compliant in performing their dialysis exchanges have hyperkalemia.²²

II. Mechanical complications:

1. Catheter malfunction: PD catheter may display obstruction either during infusion or drain phases of an exchange. Obstruction during infusion usually reflects intraluminal obstruction by fibrin or clot. Flushing by heparinized saline / thrombolytic agents is required. Distended bowel loops due to constipation often occlude holes on the distal end of the PD catheter and cause outflow problems, laxative therapy is helpful. Also adhesions due to prior peritonitis or surgery, migration of distal tip of catheter (present in abdomen rather than pelvis) and rarely fungal infections can also cause catheter obstruction.
2. Hernias and abdominal wall or genital oedema: Hernia is a relatively common complication in PD patients primarily due to increase in intra-abdominal pressures. They often present with localized painless swelling. Dialysate leakage through congenital (patent processus vaginalis) or acquired (pericatheter or prior incisional site)

abdominal wall defects results in dissection of dialysate through soft tissue and fascial planes. These present as scrotal / labial oedema or generalized abdominal wall swelling.²³ These complications require temporary cessation of PD or a switch to NIPD. Surgical repair is nearly always necessary.

3. Hydrothorax: It is a rare complication of PD, more common in females and right side (90%). Peritoneal dialysate transits the diaphragm via congenital diaphragmatic defects or lymphatics. Patient requires thoracocentesis for temporary relief of symptoms, lower volumes or NIPD, pleurodesis and sometimes surgical repair.
4. Ultrafiltration (UF) failures: Problem with UF failure may be transient (commonly due to peritonitis) or long standing. Inadequate UF leading to fluid overload is one of the commonest problems associated with long term PD. After ruling out causes like non-compliance, loss of residual renal function, dialysate leak and catheter malposition, PET should be performed. If PET suggests high or high average transporter status, it is classified as type I UF failure. These patients require short dwell periods and / or cyclers. If PET suggests low transporter status, it is classified as type II UF failure. It is due to sclerosing peritonitis and requires a permanent switch to haemodialysis.

In summary CAPD can be an equally good option of treatment of ESRD for an appropriately selected patient.

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