Seminar

Peritoneal dialysis

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Peritoneal dialysis has now become an established form of renal replacement therapy; nearly half the patients on dialysis in the UK are treated in this way. Survival of patients is now equal to that with haemodialysis. However, long-term peritoneal dialysis (>8 years) is limited to a small percentage of patients because of dropout to haemodialysis for inherent complications of peritoneal dialysis—peritonitis, peritoneal access, inadequate dialysis, and patient-related factors. However, improvements in the understanding of the pathophysiological processes involving the peritoneal membrane have paved the way for advances in the delivery of adequate dialysis, more biocompatible dialysis fluids, and automated peritoneal dialysis. Other technical advances have led to a reduction in peritonitis. Peritoneal dialysis is an important dialysis modality and should be used as an integral part of RRT programmes.

Peritoneal dialysis is now an established form of therapy in the management of end-stage renal failure (ESRF), but more than a century of painstaking work and research was needed to establish it. In 1959, Maxwell and colleagues[1] described a simplified method of intermittent irrigation of the peritoneal cavity, which used a single, disposable catheter and commercially prepared dialysis solutions. An important advance was the use of a permanent, indwelling, silicone-rubber catheter with two Dacron cuffs.[2] Despite this advance, intermittent, periodic peritoneal dialysis was regarded as having little place in the treatment of ESRF. Popovich and colleagues[3] introduced the concept of a "portable/wearable equilibration" technique for peritoneal dialysis. This approach of continuous slow therapy was developed into the currently accepted continuous ambulatory peritoneal dialysis (CAPD). At the end of 1997, the estimated number of patients worldwide on peritoneal dialysis was 120 000, about 15% of the total number of patients on dialysis worldwide.

Process of peritoneal dialysis

In peritoneal dialysis, there is exchange of solutes and fluid between the peritoneal capillary blood and the dialysis solution in the peritoneal cavity across the peritoneal membrane, which consists of a vascular wall, the interstitium, and the mesothelium. Solute movement follows physical laws of diffusion and convective transport, and fluid shifts relate to osmosis created by the addition of appropriate osmotic agents in peritoneal dialysis solutions. The crucial components of the peritoneal dialysis system are peritoneal blood flow, the highly vascular membrane, and the flow rate and volume of the peritoneal dialysis solutions. Since neither peritoneal blood flow nor the vascularity of the membrane can be manipulated, the only factor that can be adjusted to achieve maximum solute and fluid removal is the flow rate of the dialysis solutions. Various techniques and regimens have now emerged that enhance these transport characteristics.

The diffusibility of solutes also depends on the permeability of the peritoneal membrane. It is not a semipermeable membrane and thus not likely to differ substantially from the more permeable of the manufactured membranes currently used in haemodialysis. A crude measure of the size and number of holes in the membrane is given by the peritoneal equilibration test,[4] which classifies the membrane's transporter status on the basis of the rate of movement of small molecules (creatinine and glucose) across the peritoneal membrane. High transporter status indicates a highly permeable membrane that allows rapid solute transport but has limited capacity to maintain an osmotic gradient and removal of fluid (ultrafiltration) for long-dwell peritoneal dialysis. The reverse is true for a low transporter status.

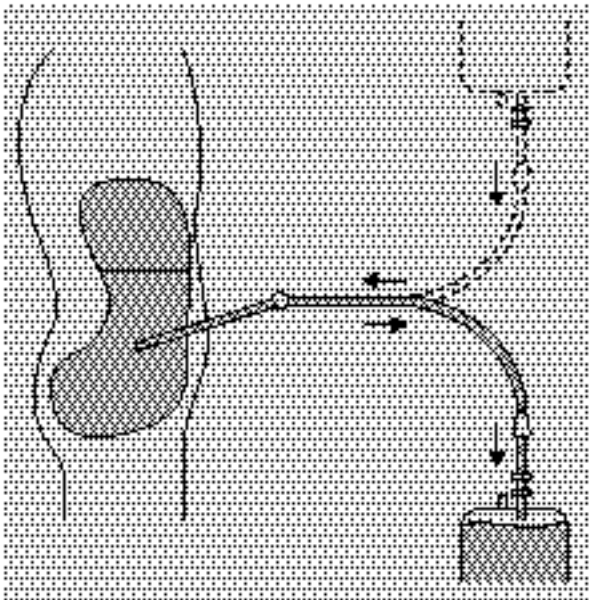

Figure 1: **Diagrammatic representation of fill and drain phases of CAPD**

Process of CAPD

Concept

The physiological basis of dialysis across the peritoneum involves diffusion, convective transport, and osmosis. The concept of CAPD modelled by Popovich and colleagues[3] uses the smallest volume of dialysate—ie, the lowest dialysate flow rate to prevent uraemia. Using a double-pool (the body as one pool and fluid in the peritoneal cavity as the other) model, they showed that the accumulation of a metabolite in the body is equal to the generation rate, minus the combined effect of the residual renal function

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Panel 1: **Advantages and disadvantages of CAPD in comparison with haemodialysis**

Advantages

Home dialysis therapy without complex machine
Easy to teach and place on home therapy
Easier for travel, more liberal diet and fluid allowance
Cheaper than haemodialysis
More suitable for children, elderly people, and patients with diabetes or cardiovascular instability
Continuous fluid and solute removal
Longer preservation of residual renal function

Disadvantages

Infections, metabolic and mechanical complications
Risk of inadequate dialysis/limited possibilities to increase adequacy
Malnutrition
Long-term viability
Psychological problems related to indwelling catheter
Fatigue from continuous use, especially in elderly people

and overall dialysate clearance. Popovich and colleagues postulated that a patient will maintain a steady-state urea concentration of about 30 mmol/L, if a volume of 10 L peritoneal dialysis fluid is equilibrated with body fluids. The CAPD technique therefore consists of four exchanges per day of 2 L or more to produce, with ultrafiltration, a total dialysate of about 10 L daily. The size of the patient is another important factor in achievement of solute-clearance targets.[5]

If 2 L of fluid is allowed to dwell in the peritoneal cavity until equilibration has been achieved, the drain volume will equal the urea clearance. During this dwell period substances of molecular weight greater than 500 Da are dialysed continuously, since the concentration gradient between the blood and the dialysate will be maintained for an extended period. Therefore CAPD is roughly six times more efficient in removing very large molecules (>5000 Da) than intermittent haemodialysis carried out for 15 h per week with cellulose membranes. High-flux haemodialysis membranes are more efficient and remove substantially more of these high-molecular-weight substances.

Technical characteristics

CAPD entails a closed system (figure 1), in which fluid is initially instilled by gravity into the peritoneal cavity and then drained out after several hours. The basic CAPD system consists of a plastic bag containing 0·5–3·0 L peritoneal dialysis fluid, a transfer set, and a permanent, indwelling, silastic Tenckhoff catheter. Various catheters are available, with differing intraperitoneal and extraperitoneal portions, designed to keep complications to a minimum; no particular catheter has been shown to be superior.[6] The connection between the bag and the transfer set is broken three or four times a day and the procedure must be carried out by a strict, sterile, non-touch technique. About 1500 exchanges per year are needed. The most common connection device is based on the Y system (disconnect).[7] With this system the effluent is drained after the connection is made with the new bag; therefore any touch contamination can be flushed out by the effluent before new fluid enters the peritoneal cavity. This system (flush before fill principle) is associated with a lower incidence of infection and means that the patient does not have to carry the empty bag and transfer set, as is the case with the older, original non-disconnect system.

Standard solutions

The solutions contain glucose as an osmotic agent and lactate, sodium, potassium, and calcium in differing concentrations. Use of acetate as a buffer has been discontinued because it is associated with loss of ultrafiltration and sclerosing peritonitis.[8] The pH of lactate-based solutions varies between 5·0 and 5·5. Lactate in dialysis solutions is therefore being replaced by bicarbonate, which is an ideal buffer for peritoneal dialysis.[9] The use of glucose makes the solution hyperosmolar and therefore unphysiological and bioincompatible. Glucose remains the most commonly used osmotic agent. Although it is cheap and safe and has been used for a long time, its absorption leads to short-lived ultrafiltration, and metabolic complications of hyperinsulinaemia, hyperlipidaemia, and weight gain resulting from the loading of 100–200 g glucose per day.[10] The hyperosmolarity and low pH of the solution have adverse effects on the mesothelium and macrophages. Glycation of the stromal proteins to form advanced glycation end-products further damages the peritoneum.[11,12] Much effort has gone into the search for an alternative osmotic agent. Icodextrin (glucose polymers) is isosmotic to uraemic plasma and produces ultrafiltration by colloid osmosis even at dwell periods of up to 12 h.[13] The other option is a mixture of aminoacids, which is promoted mainly as a protein supplement in malnourished patients.[14] Both these substances, however, can be used only intermittently, alternating with standard glucose. In future, all exchanges should be done with mixtures of these osmotic agents and bicarbonate, which are more physiological than currently used solutions.

Advantages and disadvantages of CAPD

The main advantage of CAPD is that it is relatively simple to teach, so the patient can quickly be established on home dialytic therapy (panel 1). Unlike haemodialysis, CAPD does not require specific and complex equipment, and the therapy results in continuous steady-state biochemical and fluid status, thus avoiding the see-saw fluctuations of intermittent haemodialysis.[15] CAPD is at least 25% cheaper than in-hospital haemodialysis, with hospital costs included. It is also more appropriate for patients with

	Time (years)	Proportion of patients surviving (%)		Proportion of patients continuing with treatment (%)	
		CAPD	HD	CAPD	HD
Study					
Charytan (1986)	2	80	82	32	34
Burton (1987)	2	84	82	..	..
	10	45	45	..	..
Gokal (1987)	4	62	74	61	91
Serkes (1990)	2	83	75	67	93
Maiorca (1991)	6	75	84	87	93
Cavali (1989)	3	71	58	75	73
Maiorca (1995)[16]	10	50	50	95	50
Registries					
Australia (Disney 1995)	3	73	57	..	..
Italian (Lupo et al 1994)	5	42	54	..	..
European Dialysis and Transplant Association (Mallick et al 1995)	10	30	36	..	..
Canada (Fenton et al 1997)	5	35	36	..	..
United States Renal Data System (Held et al 1994)	2	78	78	..	..
Japan (Teraoka 1995)	5	..	60	..	..

Studies listed in Further reading, at end of paper.

Comparison of outcomes of CAPD and haemodialysis (HD)

Panel 2: **Complications of CAPD**

Mechanical effects
Abdominal-wall hernia
Haemorrhoids
Back pain
Fluid leaks—oedema of external genitalia, hydrothorax
Respiratory problems especially in patients with pre-existing chest disorders
Abdominal fullness, occasional pain with drainage of fluid
Constipation
Increased vascular insufficiency
Catheter malpositions

Infections
Peritonitis
Infection at catheter exit
Tunnel infections

Metabolic complications
Obesity, hyperlipidaemia with glucose loading
Loss of appetite from glucose absorption
Protein and aminoacid losses

Peritoneal membrane damage
Development of hyperpermeable or hypopermeable changes
Peritoneal membrane sclerosis
Impairment of peritoneal host defence

diabetes because insulin given intraperitoneally gives better control of blood sugar than does insulin administered by other routes. Children and patients with severe cardiovascular disability are also better suited to CAPD than to haemodialysis.

The main disadvantages relate to infections, mechanical and metabolic complications inherent in the technique, and a higher rate of technique failure and need to transfer to haemodialysis.[16] There is also burn-out from long-term use of the treatment, especially in elderly patients.[17]

Outcome of peritoneal dialysis

The outcome can be defined in terms of survival of patients, retention on CAPD, morbidity (eg, hospital admission), and quality of life. Various studies (table) have shown that survival is similar on haemodialysis and peritoneal dialysis. 50–60% of deaths have cardiovascular causes. Contributing factors include uraemia, anaemia, hypertension, fluid overload, and hyperlipidaemia.[18] However, patients are more likely to persist with haemodialysis than with peritoneal dialysis.[19] Hospital admission is marginally more likely for patients on peritoneal dialysis.[20] The dialytic therapies do not differ in the various measures of quality of life. All are inferior to successful transplantation.[21] Both haemodialysis and peritoneal dialysis limit social life and leisure and sexual activity in about 60% of patients.[22] Only about 1–4% of patients who start peritoneal dialysis continue for longer than 8 years.[23] The high drop-out rate is due to technique-related complications. There is concern about the integrity of the peritoneal membrane with long-term use. Patients with hyperpermeable membranes have poorer outcomes,[24] as do malnourished patients.

Complications of CAPD (panel 2)

Peritonitis

Peritonitis is an important source of morbidity and leads to change of treatment to haemodialysis. The incidence of peritonitis has fallen substantially with the development of adequate delivery systems and connectors.[25]

The frequently repeated drainage of the peritoneal dialysis effluent allows early detection of peritoneal inflammation. For both patient and doctor, the turbidity of the effluent is the earliest sign of a probable infection. The main site for infection of the peritoneal cavity is through the lumen of the catheter (touch contamination at time of exchanges) or around the outside of the catheter (related to the exit site and tunnel). 75% of episodes are caused by gram-positive organisms; *Staphylococcus epidermidis* accounts for 50%. Serious infections are caused by *S aureus,* pseudomonas species, and fungal organisms, especially when associated with exit-site or catheter-tunnel infections.

The main pathogenetic mechanism for peritonitis is catheter colonisation by *S epidermidis* and the suppression of local peritoneal defence mechanisms (chemotaxis, opsonisation, cytokine release). The risk of developing peritonitis, therefore, rests on the delicate balance between colonisation of the CAPD system, the quantity of bacteria invading the peritoneal cavity by whatever route, and the local peritoneal defence mechanism.

Treatment is by intraperitoneal antibiotics, which are usually self-administered by patients. Up to 80% of episodes can be managed entirely at home.[25,26] With current disconnect systems, a peritonitis rate of one episode every 2–3 years of therapy for an individual patient can be achieved.[27] Repeated attacks of peritonitis damage the peritoneal membrane, resulting in permeability changes and poorer outcomes. Repeated or persistent peritonitis may necessitate temporary or permanent catheter withdrawal and is one of the main reasons for technique failure.

Nutritional disorders

With long-term CAPD, several harmful metabolic factors have emerged, including low rates of removal of low-molecular-weight nitrogenous waste products, loss of protein, aminoacids, and other nutrients into the dialysate (up to 15 g per 24 h), and an inadequate nutritional intake. Protein and aminoacid losses increase in peritonitis. These observations raise questions about the long-term metabolic and nutritional consequences of CAPD.[23] About 10% of patients are severely malnourished, and a further 30% have mild to moderate malnutrition.[28] Contributory factors include low nutrient intake, impaired appetite, abdominal fullness, delayed gastric emptying (especially in patients with diabetes, who may have gastroparesis), glucose absorption, and inappropriate removal of uraemic metabolites.[29] The effect of decreasing residual renal function is important in provision of adequate dialysis; it is associated with a decrease in protein intake,[30] which can be overcome by dietary supplements, use of aminoacid-containing dialysis solutions,[14] and optimisation of solute clearance.

Malnutrition increases the risk of morbidity and mortality for all dialysis patients. Patients with serum albumin concentrations below 35 g/L have a significantly higher death rate than patients with concentrations above this value.[31]

Adequacy of dialysis

Although the clearance of low-molecular-weight solutes is lower with peritoneal dialysis than with haemodialysis, the peritoneal method provides effective control of uraemia and electrolyte disturbances of chronic renal failure.

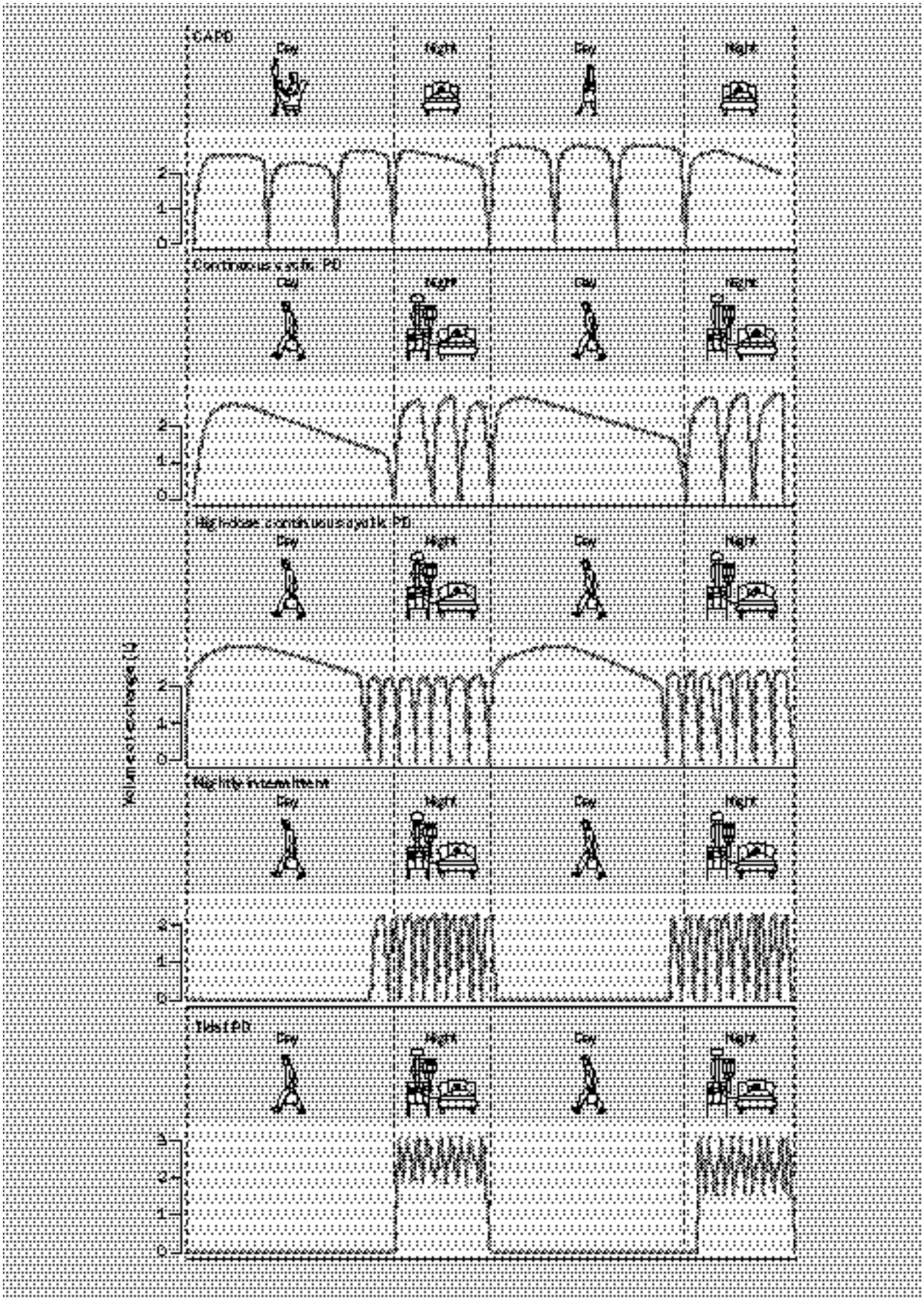

Figure 2: **Various APD regimens compared with standard CAPD**
Reproduced with permission from Khanna and colleagues.[38]

Clearance of low-molecular-weight solutes is affected by various factors, the most important of which are the size of the patient, peritoneal permeability, and the residual renal function.[32] The clinician must take these factors into account in arriving at a prescription, which needs to be tailored to the individual. The daily standard regimen of four 2 L exchanges has been applied in up to 90% of patients worldwide without regard to these important factors. This practice must change.

The measures used to assess adequacy of dialysis are the fractional clearance of urea (urea clearance per unit time related to total body water—Kt/V) and creatinine clearance (both peritoneal and residual renal). Various national and international bodies have set minimum targets for these solute clearances. The National Kidney Foundation in USA has set a target minimum urea clearance of 2·0 and total creatinine clearance of 60 L per week.[33] These targets are greater than those set by the British Renal Association of (>1·7 and >50, respectively).[34] The discrepancy is related to a lack of conclusive evidence for the US guidelines, which are based mostly on a prospective cohort study of new CAPD patients in Canada and the USA which give theoretical links between adequacy and outcome.[35]

Failure to achieve these targets can lead to uraemia, decreased protein intake, and increased risk of death.[36] A weekly Kt/V of 1·9 for CAPD patients is roughly equivalent to a weekly urea Kt/V of 3·0 for haemodialysis (three treatments per week).[37]

The overall clearance capacity of the peritoneal cavity for clearance of low-molecular-weight solutes is limited by the volume of dialysis fluid that can be prescribed. The standard prescription (four exchanges of 2 L daily) is likely to be inappropriate for patients of bodyweight greater than 80 kg, especially when residual function is negligible after 3–4 years of therapy.[35] The clinician therefore must adjust the prescription for the individual to meet both minimum targets and the patient's lifestyle preference. Exchanges of larger volumes (2·5–3·0 L) can improve solute removal but this approach may be constrained by the patient's intolerance of these large volumes (sensation of fullness, aching, and dyspnoea). Peritoneal clearance can, however, be enhanced by the use of automated peritoneal dialysis (APD).

APD

APD refers to all forms of peritoneal dialysis that use a mechanical device to assist in the delivery and drainage of the dialysate from the peritoneal cavity (figure 2).[38,39] The most obvious advantage of APD is that it obviates the need for intensive manual involvement and limits the process of peritoneal dialysis to two procedures—setting up of the dialysis regimen with an initial connection of the catheter to the machines and disconnection from the patient with dismantling of the machine at the end of dialysis. It is a home-based therapy and is predominantly done during the night. Thus, the patient and helper are free during the day with short-dwell cycles run in and out of the peritoneal cavity by the cycler machine. However, because of the need to provide additional dialysis to achieve adequacy targets, daytime exchanges have also become necessary, thereby complicating the procedure and intruding in the patient's daytime routine. APD is much more expensive than CAPD. Nevertheless, over the past 5 years APD has been the fastest-growing method of renal replacement therapy; over the past 3 years the number of patients on this therapy has doubled to nearly 30 000 worldwide.

The selection of APD rather than CAPD is mostly influenced by the patient's preference and lifestyle needs, the physician's advice and predictions, the availability of equipment and supplies, and the patient's clinical state—for example, a hyperpermeable membrane makes long-dwell CAPD difficult because of the problems of removing adequate amounts of fluid, even though solute clearance may be increased. The most important consideration in the selection of APD other than the patient's preference is the individual's peritoneal solute transporter status. Patients with high rates of solute transport (hyperpermeable) require more frequent cycles of short duration to accomplish ultrafiltration. Nightly intermittent peritoneal dialysis is the therapy of choice in this instance. Heavy patients and those with greater dietary protein intake require greater clearance of small solutes; high-flow APD is recommended for their treatment. For patients with low peritoneal permeability, peritoneal dialysis therapy may be inappropriate, especially when there is very little residual renal function. These patients are unable to remove adequate amounts of solute and are best managed with haemodialysis.[36]

Future of peritoneal dialysis and renal replacement therapy

There has been a huge expansion in both the clinical and research areas of peritoneal dialysis over the past 20 years. The technique is now used worldwide, mainly in the form of CAPD, but the use of APD is increasing. Data on long-term survival are lacking, and only a limited number of patients have been on peritoneal dialysis for longer than 10 years. Success is dependent on the long-term viability of the peritoneal membrane and lies in preserving the peritoneum as a dialysing membrane for as long as possible. High-risk patients caring for themselves with peritoneal dialysis in the community need a lot of psychosocial support, especially elderly people, patients with diabetes, and those who are socially isolated. Since these groups will increasingly be referred for dialysis therapy in the future, their full rehabilitation is going to be very important and will have resource implications.

An appropriate approach is to use peritoneal dialysis as an initial form of dialytic therapy until transplantation or until the treatment becomes inappropriate (which is about 5 years from the time of starting dialysis in most patients). The main difficulties of adequate access, the risk of peritonitis, and inadequate nutrition must be resolved.

Each method of treatment for renal failure must be considered as part of an integrated approach rather than as a stand-alone treatment. Each patient may experience all forms of treatment, and some may receive one type of treatment for more than one period as medical and social circumstances change. Peritoneal dialysis and haemodialysis must be available. For patients on peritoneal dialysis, back-up haemodialysis is essential during episodes of infection, or if the treatment fails abruptly.

If a transplant eventually fails, provision must be made for patients to resume dialysis; the patient needs to be counselled about this possibility. The best results are obtained with a coordinated programme that integrates all three approaches, based on clinical needs and those of the patient.

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