INVITED ARTICLE

PERITONEAL DIALYSIS — A REVIEW WITH CONSIDERATION OF THE ROLE OF CAPD IN RENAL REPLACEMENT THERAPY IN DEVELOPING COUNTRIES

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INTRODUCTION

The advent of the soft silicon-rubber catheter (1) in the 1960s made maintenance peritoneal dialysis feasible. Nevertheless, peritoneal dialysis has been regarded as inferior to haemodialysis and is often used to 'hold' patients while preparations are being made for maintenance haemodialysis or only reserved for those patients, who, for medical or social reasons, are considered unsuitable candidates for long term haemodialysis.

FACTORS GOVERNING TRANSPERITONEAL SOLUTE

Compared with haemodialysis, peritoneal dialysis is inefficient at removing small molecules such as urea and creatinine. To maintain satisfactory biochemistry, a patient on intermittent peritoneal dialysis has to spend on the average 48 hours a week on dialysis exchanging 100 litres of fluid, due mainly to the resistance a solute has to overcome while traversing the tissue layers from the vascular compartment into the peritoneal cavity. Transperitoneal transfer of solutes is a simple process of diffusion (2). In the absence of ultrafiltration, molecules diffuse across the peritoneal membrane down the concentration gradient.

The rate of diffusion of a molecule is inversely proportional to the square root of its molecular weight (2), or more accurately, the molecular size. An inverse linear relation is apparent when the transperitoneal clearances of various solutes are plotted against their respective molecular weights on a semi-logarithmic scale (3). The effective molecular size of a solute can be modified by physicochemical forces such as surface electrostatic charges attracting a 'shell' of water of hydration, or by covalent binding to plasma proteins. The low transperitoneal clearance of phosphate is generally attributed to the water of hydration the radical carries. The distribution of a particle across the semipermeable peritoneum at equilibrium is also affected by the Gibbs-Donan effect. One can do little to change the molecular characteristics of a solute. Thus efforts to improve the efficiency of peritoneal dialysis have concentrated on the other factors which influence transperitoneal solute clearances.

PERITONEAL BLOOD FLOW

The clearance of small molecules depends to some extent on peritoneal blood flow. The blood supply to the visceral peritoneum is derived from the splanchnic circulation. Splanchic blood flow averages 1500 ml/min (4) , far exceeding the usual 200 ml/min obtained with arteriovenous fistulae used for haemodialysis. However, a proportion of the blood flow is to the viscera and probably never involved in solute exchanges across the peritoneal membrane. Attempts to improve the efficiency of peritoneal dialysis have included the use of pharmacological agents such as sodium dioctylsuccinate (5), dopamine (6), sodium nitroprusside (7) and various gut hormones (8). The agent which produces the most remarkable increase in transperitoneal clearance of solutes is nitroprusside. At the recommended dose, hypotensive effects are appreciable and the modest, though significant increase in the transperitoneal clearances of urea and creatinine is probably not worth the increased protein loss in the dialysate (7). Blood flow to the peritoneum is probably optimal (9) and not an important limiting factor in transperitoneal solute clearances. Nevertheless, in special clinical situations, vasoactive agents have been used successfully to increase transperitoneal solute clearances (10).

DIALYSATE FLOW RATE

The usual dialysate flow rate employed in intermittent peritoneal dialysis is about 30 ml/min compared to the 500 ml/min in haemodialysis. However, even when the dialysate flow rate is increased to above 200 ml/min, the transperitoneal urea clearance does not exceed 40 ml/min (11). Evidently the resistance to diffusion offered by the stagnant fluid film adjacent to the peritoneal membrane is not a limiting factor. The major resistance to diffusion resides in the intervening tissue layers between the vascular compartment and the mesothelial cell of the peritoneum. Increasing the rate of dialysate flow increases the cost of treatment enormously. To reduce the cost, devices for the regeneration of the dialysate are needed and the major attraction of peritoneal dialysis, simplicity, is lost.

AREA AND PERMEABILITY OF PERITONEAL MEMBRANE, ULTRAFILTRATION AND SOLVENT DRAG

The anatomical area of the peritoneal membrane has been quoted as being equivalent to the total surface area of the glomerular capillaries of both kidney (12). However, its functional area is probably less than that of a standard 1 m2 artificial kidney (12). One way in which vasoactive agents such as nitroprusside act is to open up unperfused capillaries and thereby increase the functional area of the membrane involved in solute exchanges. Hypertonic glucose solutions increase the ultrafiltration rate and by the phenomenon of 'solvent drag' increase transperitoneal solute clearances (13). The fact that inulin clearance increases more than urea clearance implies that the membrane becomes more permeable. The effect persists for some time after the hypertonic fluid has been exchanged. By alternating hypertonic with hypotonic solutions, the transperitoneal urea clearance can be increased (14).

CONTINUOUS AMBULATORY PERITONEAL DIALYSIS (CAPD)

Is it possible to turn the low transperitoneal clearances into an advantage? Popovich et al (15) first introduced continuous ambulatory peritoneal dialysis and the technique has since been popularised thanks to Oreopoulos and his co-workers (16, 17). The equilibration of peritoneal dialysis solution with plasma increases with time (18). At the end of 4 hours almost 100% equilibration is reached for urea. Thus it is possible to predict plasma concentrations of small molecules such as urea and creatinine by measuring their concentrations in the residual peritoneal fluid left overnight, before the next dialysis is commenced (19). In CAPD, dialysis is continuously taking place across the small concentration gradient that persists throughout the period the dialysis solution is allowed to dwell in the peritoneal cavity. Thus the low transperitoneal solute transfer rates are used to the patient's advantage, rendering it possible for the patient to be ambulant during dialysis. The potential advantages of the technique are:

1. It is simple and less able patients may be able to cope with the procedure.
2. The patient is ambulatory during treatment and rehabilitation is easier.
3. The dialysis is more gentle and physiological.
4. No dietary restriction is needed.
5. The procedure is less expensive than haemodialysis.

Since its introduction, most renal centres have experimented with the technique. In Europe alone, almost 3000 patients had received CAPD by the end of 1982 (20), four years after CAPD was introduced. Has CAPD really revolutionalized (16) the treatment of chronic renal failure? Experience to date confirms that the technique provided satisfactory dialysis. A steady state is reached and CAPD patients do not have the large fluctuations in haemodynamics and biochemistry as experienced by patients on intermittent haemodialysis. The mean haematocrit of patients on CAPD is higher than that of haemodialysis patients (21) and in individual patients a progressive rise in haematocrit is usually apparent (22). Compared to haemodialysis, the weekly clearance of urea and creatinine by CAPD is lower. However, the clearance of inulin and B12, the so-called 'middle molecules', far exceeds that obtained with conventional haemodialysis (17). The state of well-being of patients on CAPD supports the contention that uraemic toxins are 'middl molecules'. There is little doubt that CAPD has expanded the therapeutic options for the manage-

ment of end-stage renal disease and has enabled many patients who would have been denied haemodialysis to cope with their renal failure. Unfortunately, CAPD can be more expensive than haemodialysis either in terms of the number of days of hospitalization or in terms of the cost of antibiotic therapy (20). Even the cost of the dialysis solutions alone is more expensive than the recurrent costs of home haemodialysis. Although hyperkalaemia is seldom encountered, it is erroneous to allow CAPD patients liberal fluid intake. Liberal fluid intake necessitates the frequent use of hypertonic glucose solutions to remove the excess water from the body. Gross obesity (23) results because glucose in the dialysate is an important source of calories (24). Hyperlipidaemia, common in uraemic patients, persists in CAPD.

About 10% of patients develop abdominal hernias (21, 23), sometimes complicated by fatal intestinal strangulation. Transperitoneal clearance of B12 can potentially lead to a deficiency state (21). Uraemic polyneuropathy improves but renal osteodystrophy may progress. Loss of ultrafiltration occurs in some patients after a period of CAPD, either as a result of sclerosis of the peritoneum owing to repeated peritonitis or related to the use of acetate solutions (25). Although the technique appears simple, CAPD can be extremely labour-intensive. Peritonitis remains an insoluble probelm and averages 1 to 3 episodes per patient year, although some units have better results (23). There is no difference in the incidence of peritonitis whether CAPD is used as a first choice treatment or an alternative treatment to haemodialysis (20). Nor does the age of the patient seem to matter. Some units have employed bacterial filters in the infusate line to reduce the incidence of peritonitis (26). Others have introduced innovations in the "connectology" of the dialysis fluid delivery system (27). Recently, a device which enables aseptic connection to be made in the presence of ultraviolet light has become commercially available. The diversity of the measures taken to reduce the incidence of peritonitis is itself an indication of the amplitude of the perpetual threat.

WHAT IS THE ROLE OF PERITONEAL DIALYSIS IN DEVELOPING COUNTRIES?

Treatment of end-stage renal disease is expensive, although certainly more rewarding and probably no more expensive than other 'end-stage' diseases such as malignancies. Although hospital-based haemodialysis is a simple and sure way out for the patient with end-stage renal failure, the lack of trained personnel and financial resources in developing countries precludes the widespread deployment of hospital haemodialysis. Home haemodialysis is the least expensive. However, in developing countries where the level of education of the patient is low and the housing situation unsatisfactory, it is difficult to push for home haemodialysis. The emotional stress of having to handle 'technically complicated' haemodialysis at home is too much for the patient and his relatives. The need for a helper to dialyse the patient means that for 2 to 3 days a week, two individuals are involved in the procedure. In countries where there is no comprehensive social welfare programme, 2 to 3 days a week off work means permanent unemployment. CAPD can play an important role in renal replacement programmes in developing countries. There is no danger of aluminium toxicity which results from the aluminium in piped water. The patient is ambulant during treatment and full-time employment is possible. The patient's biochemistry can be monitored by sampling residual peritoneal fluid. The patient can take care of himself and a helper is not needed. Even though peritonitis poses a constant threat, a considerable number of patients have never had peritonitis (21, 26). CAPD is especially valuable for housewives. Although 4 exchanges each of 2 liters are often spaced out in 24 hours in CAPD, experience in treating Chinese patients (30 patients to date) suggests that 3 exchanges a day are sufficient to maintain the patient in good health. The exchanges are carried out at 8am, 5pm and 11pm. The exact schedule can be slightly manipulated to suit the patient's own social engagements. Patients can be transplanted while on CAPD without going through the rictuals of haemodialysis. Currently 3 exchanges a day cost $13 dollars (US) and with some financial assistance from the government or charitable organizations, most patients can afford the treatment.

It must be remembered that even in the most experienced units the technique failure rate of CAPD is disappointingly high, approaching 30% by 2 years (23). There must therefore be haemodialysis facilities available to back.up the treatment in case CAPD fails. CAPD may be regarded as the treatment of choice for diabetic patients in end-stage renal failure. Some patients may prefer to carry out peritoneal dialysis at night with the help of automatic cycling devices. To establish a comprehensive renal replacement programme, haemodialysis, peritoneal dialysis and renal transplantation must each be given its own deserved place. This is no easy job because rumour has often been spread, intentionally or unintentionally, by patients and physicians alike, that peritoneal dialysis is a second rate treatment to haemodialysis. That about 30% of patients on dialysis in the United Kingdom, Australia and Canada are treated with CAPD (28) is good enough reason for nephrologists in developing countries to have a careful look at the technique. By adapting the technique to suit the circumstances and requirements of their individual countries, they can contribute to the development of an important mode of treatment for end-stage renal failure.

REFERENCES

1. Tenckhoff H, Schechter H: A bacteriologically safe peritoneal access device. Trans Am Soc Artif Intern Organs 1968; 14:181-7.
2. Aune S: Transperitoneal exchange, I. Peritoneal permeability studied by transperitoneal plasma clearance of urea, PAH, inulin and serum albumin in rabbits. Scan J Gastroenterol 1970; 5:85-97.
3. Maher F, Hirszel P: Augmenting peritoneal mass transport. Int J Artif Organs 1979; 2:59-68.
4. Wade OL, Combes B, Childs AW, Wheeler HO, Cournard A, Bradley SE: The effect of exertion on the splanchnic blood volume in normal man. Clin Sci 1956; 15:457-63.
5. Penzotti SC, Mattocks AM: Effects of dwell time, volume of dialysis fluid and added accelerators on peritoneal dialysis of urea. J Pharm Sci 1971; 60:1520-2.
6. Chan MK, Varghese Z, Baillod RA, Moorhead JF: Peritoneal dialysis: effect of intraperitoneal dopamine. Dialysis & Transplantation 1980; 9:382-4.
7. Nolph KD, Ghods AJ, Brown P, et al: Effects of nitroprusside on peritoneal mass transfer coefficients and microvascular physiology. Trans Am Soc Artif Intern Organs 1977; 23:210-8.
8. Maher JF: Peritoneal transport rates: mechanism, limitations and methods for augmentation. Kidney Int [Suppl] 1980; suppl 10:S117-20.
9. Aune S: Transperitoneal exchange: II. Peritoneal blood

flow estimated by hydrogen gas clearance. Scand J Gastroenterol 1970; 5:99-104.
10. Brown ST, Ahearn DJ, Nolph KD: Reduced peritoneal clearances in scleroderma increased with intraperitoneal isoproterenol. Ann Intern Med 1973; 78:891-4.
11. Nolph KD, Popovich RP, Ghods AJ, Twardowski Z: Determinants of low clearances of small solutes during peritoneal dialysis. Kidney Int 1978; 13:117-23.
12. Henderson LW: The problem of peritoneal membrane, area and permeability. Kidney Int 1973; 3:409-10.
13. Henderson LW, Nolph KD: Altered permeability of the peritoneal membrane after using hypertonic peritoneal dialysis fluid. J Clin Invest 1969; 48:992-1001.
14. Zelman A, Gisser D, Whittam PJ, Parsons RH, Schuyler R: Augmentation of peritoneal dialysis efficiency with programmed hyperhypo-osmotic dialysates. Trans Am Soc Artif Intern Organs 1977; 23:203-9.
15. Popovich RP, Moncrief JW, Nolph KD, Ghods AJ, Twardowski ZT, Pyle WK: Continuous ambulatory peritoneal dialysis. Ann Intern Med 1978; 88:449-56.
16. Robson HD, Oreopoulos DG: Continuous ambulatory peritoneal dialysis: A revolution in the treatment of chronic renal failure. Dialysis & Transplantation 1978; 7:99-1004.
17. Oreopoulos DG, Robson M, Fuller B, Ogilvie R, Rapaport A, De Veber GA: Continuous ambulatory peritoneal dialysis: a new era in the treatment of chronic renal failure. Clin Nephrol 1979; 11:125-28.
18. Boen ST: Knetics of peritoneal dialysis — a comparison with the artificial kidney. Medicine (Baltimore) 1961; 40:243-87.
19. Chan MK, Huang TC, Varghese Z, Baillod RA, Moorhead JF: Predicting plasma concentrations of common biochemical values from residual peritoneal fluid in patients on peritoneal dialysis. Br Med J 1978; i:1670-1.
20. Broger M, Brunner FP, Brynger H, Donckerwolcke RA, Jacobs C, Kramer P, Selwood NH, Wing AJ: Combined report on regular dialysis and transplantation in Europe XII, 1981. Proc Eur Dial Transplant Assoc 1982; 19:20-59.
21. Chan MK, Baillod RA, Chuah P, et al: Three years' experience of continuous ambulatory peritoneal dialysis. The Lancet 1981: i:1409-12.
22. Gokal R, McHugh M, Fryer R, Ward MK, Kerr DNS: Continuous ambulatory peritoneal dialysis: one year's experience in a UK dialysis unit. Br Med J 1980; iii:474-7.
23. Khanna R, Oreopoulos DG, Dombros N, et al: Continuous ambulatory peritoneal dialysis (CAPD) after the e years: still a promising treatment. Peritoneal Dialysis Bulletin 1981; 1:24-34.
24. DeSanto NG, Capodicasa G, Senatore R: Glucose utilization from dialysate in patients on continuous ambulatory peritoneal dialysis (CAPD). Int J Artif Organs 1979; 2:119-24.
25. Rottembourg J, Gahl GM, Poignet JL, et al: Severe abdominal complications in patients undergoing continuous ambulatory peritoneal dialysis. Proc Eur Dial Transplant Assoc 1983; 20:236-42.
26. Slingeneyer A, Mion C: Peritonitis prevention in continuous ambulatory peritoneal dialysis: long term efficacy of a bacteriological filter. Proc Eur Dial Transplant Assoc 1982; 19:388-96.
27. Maiorca R, Cantaluppi A, Cancarini GC, et al: "Y" connector system for prevention of peritonitis in CAPD: a controlled study. Proc Eur Dial Transplant Assoc 1983; 20:223-30.
28. Communication from Travenol Laboratories.