NEFROLOGIA. Vol. VIII. Suplemento 3. 1988

Continuous ambulatory peritoneal dialysis: metabolic effects

D. N. S. Kerr
Hammersmith Hospital. London.

The place of continuous ambulatory peritoneal dialysis (CAPD) in the treatment of renal failure is now well established. Two recent reports of experience at Newcastle upon Tyne [1] and in seven UK dialysis centres [2] present the typical picture in Britain now that the procedure has found a stable place in therapy. In the seven centre study, which looked at new patients starting either haemodialysis (HD) or CAPD, more than twice as many patients started CAPD. Patient survival was similar with the two techniques but treatment success was lower with CAPD i.e. more patients changed from CAPD to HD than vice versa. In both these studies the drop out rate from CAPD was about 10 % per annum, exclusing deaths and renal transplants.

Consequently CAPD must be performed in association with a haemodialysis unit to which patients who fail CAPD can be transferred. However as a preparation for renal transplant, the major goal of treatment in Britain, it is an easier and cheaper alternative than HD. Graft and patient survival from CAPD are the same as those from HD [3, 4]. However with the present restricted supply of cadaver kidneys, the majority of patients on CAPD are still waiting for a graft after 3 years [1, 2]. Consequently the long term effects of this form of treatment are becoming of major importance. The hazards of peritonitis and changes in peritoneal morphology and function will be discussed in other papers in this symposium. The third major consideration is the metabolic effects of CAPD.

Plasma sodium

CAPD controls plasma sodium within the normal range in most patients [5]. The unpublished data supporting that statement showed that in 74 patients followed for more than 6 months in Newcastle mean plasma sodium was between 136 and 138 mmol/l with about 80 % of observations in the normal range. However hyponatraemia is common during episodes of peritonitis and other infections in CAPD patients, typically in the range 120-134 mmol/l.

Fluid balance and hypertension

CAPD is probably superior to HD in controlling blood pressure. In our three year follow-up study [5] half the patients who were hypertensive on starting CAPD were able to discontinue or reduce their antihypertensives. However fluid overload is a common problem in poorly compliant patients and those with ultrafiltration failure. The increasing use of high dextrose bags to counter this fluid overload causes excessive glucose absorption and the metabolic problems discussed below. With good dietary advice and supervision this is not an inevitable problem. At Newcastle the number of "heavy" bags per 24 hours remains constant at about 0.8 throughout our 6 year study [1]. However this good result reflects the removal of the least compliant patients from CAPD to HD.

Plasma potassium

CAPD avoids the wide swings in plasma potassium that complicate HD. In our three year follow-up [5], mean plasma potassium was consistently between 4.0 and 4.5 mmol/l, three quarters of all observations were within the normal range and levels above 6.0 mmol/l were rarely encountered. This satisfactory control of plasma potassium with only moderate dietary restraint and without use of ion exchange resins is at first sight surprising. A patient with a plasma potassium of 4.5 mmol/l, using 4 two litre exchanges, and having an extra litre of ultrafiltrate per 24 hours, cannot excrete more than about 40 mmol through his peritoneum per 24 hours. The recommended intake for our patients is 60 mmol per day but the typical intake is between 50 and 80 mmol per day. Those with negligible residual renal function must excrete the remainder through the bowel. Investigators in Newcastle [6] and elsewhere [7, 8] have used the dialysis bag technique to confirm that there is a substantially raised secretion of potassium in the large bowel in patients with chronic renal failure, whether treated by HD, CAPD or conservative means.

Correspondence: D. N. S. Kerr.
Royal Postgraduate Medical School.
Hammersmith Hospital.
Du Cane Road.
London W12 OHS.
United Kingdom.

Freedom from peaks of hyperkalaemia is ensured by the stable control of acid base status during CAPD.

Plasma chloride and bicarbonate

Plasma chloride is usually maintained within the normal range; mean levels in our study [5] were between 100 and 104 mmol/l. Using Travenol Dianeal solutions containing 35 mmol/l of lactate, we observed plasma bicarbonate levels in the lower normal range, the mean results being between 23 and 25 mmol/l. The use of a 40 mmol/l lactate solution produces high normal bicarbonate levels [9]. We did not measure blood pH routinely and it has received surprisingly little attention from others. In one study using acetate as buffer at 38.5 mmol/l, blood pH was in the low normal range, around 7.35 [10]. The effects of prolonged acidosis on bone are therefore unlikely to affect patients on CAPD.

Serum magnesium

The standard dialysis fluid containing 0.75 mmol/l causes hypermagnesaemia. In our study [5] mean serum magnesium was between 1.2 and 1.3 mmol/l with a fairly wide scatter, about 10 % of samples being over 1.4 mmol/l. These are not levels which produce symptoms. The burning, itching, drowsiness and coma that characterise "hard water syndrome" following failure of a water-softener during haemodialysis are found with levels well above 3 mmol/l. The ideal serum magnesium in renal failure is a subject of inconclusive debate. In experimental models high serum magnesium protects against metastatic calcification but interferes with ossification in normal bone [11]. Since there is no evidence that CAPD patients are protected against metastatic calcification or unduly susceptible to osteomalacia(see below)it seems unlikely that these effects are important in humans. Lower serum magnesium by use of a low — or zero — magnesium haemodialysis fluid improves nerve conduction time without producing any adverse side effects [12]. Consequently some nephrologists now use CAPD fluid with a lower magnesium content of 0.25 mmol/l.

In normal subjects, raising serum magnesium above normal depressed serum PTH [13] but the effect is small or absent in the presence of severe secondary hyperparathyroidism and the consensus view is that hypermagnaesemia has little role in protecting patients against hyperparathyroidism, supporting the proposition that we should aim at normomagnesaemia in our patients. However we should avoid hypomagnesaemia which causes hypocalcaemia, and depresses parathyroid activity so that the hypocalcaemia can only be corrected by giving magnesium [13, 14]. On current, limited, evidence a dialysis fluid magnesium of 0.25 mmol/l achieves both objectives.

Serum calcium, phosphate, PTH and alkaline phosphatase

The standard dialysate with 1.75 mmol/l raises serum total and ionised calcium into the normal range [5]. In our experience, serum PTH usually falls and serum alkaline phosphatase tends towards the normal range [5, 15]. It must be emphasized, however, that these results are obtained with the help of oral phosphate binders and small doses of alfacalcidol. Without phosphate binders many of our patients do not achieve a serum phosphate in the normal range. We use calcium carbonate as first choice adding aluminium hydroxide only if increasing doses of calcium carbonate causes hypercalcaemia or fail to control serum phosphate at the limit of patient tolerance. It would be sensible at this point to add a magnesium salt such as magnesium hydroxide (which counters the constipation caused by calcium carbonate). This approach has been used successfully in haemodialysis but it requires reduction of the magnesium concentration in CAPD fluid and the limit of dosage has not been well defined in CAPD patients. Consequently we have then added aluminium hydroxide although this causes a rise in serum aluminium [5, 15, 16]. This is a resonable policy in a unit geared to renal transplant which would be unsuitable for a population expected to spend many years on CAPD since bone aluminium accumulates in proportion to total ingested dose. It requires careful monitoring even when transplant is the eventual goal since half the patients awaiting transplant are still waiting at the end of 3 years [1, 2]. In our early experience at Newcastle the intake of calcium carbonate gradually fell and the intake of aluminium hydroxide rose with time on CAPD. With a more vigorous approach to avoiding aluminium-containing antacids, we can now, at Hammersmith, keep aluminium hydroxide intake down so that only a third or less of the patients take this drug.

Bone disease

Serial studies of bone symptomatology, radiology and bone histology showed an encouraging response in our early experience [5, 15]. The grade of osteitis fibrosa fell in most patients and osteomalacia only developed in a few patients who were aluminium overloaded from previous exposure during haemodialysis, particularly after parathyroidectomy [17]. However, although CAPD,

with phosphate binders and alfacalcidol, appears to protect against bone disease in the first few years of treatment, it is not effective in controlling pre-existing severe hyperparathyroidism. Parathyroidectomy was performed on 13 of the 229 patients included in our 6 year study [1]; eight of these were patients transferred from haemodialysis or failed renal transplant who already had moderate or severe hyperparathyroidism when starting CAPD, which did not regress on treatment. Studies from other centres have shown considerable variation in the progress of bone disease during CAPD which probably reflects variations in the diet, medications and past experience of the patients as well as variations in technique and composition of the dialysis fluid.

Metastatic calcification

In our experience, metastatic calcification in soft tissues, small and large blood vessels has continued to develop in patients on CAPD despite generally good control of serum calcium and phosphate levels. We found no relationship between the Ca X P product or the serum PTH and the progression of metastatic calcification, in contrast to these well established relationships in renal failure treated conservatively [18]. The possibility therefore exists that other factors such as oxalate retention contribute to metastatic calcification during CAPD; this is the subject of a current investigation by my former colleagues in Newcastle upon Tyne.

Carbohydrate metabolism

Dextrose is absorbed from CAPD fluid in direct relationship to the infused concentration and volume [19]. Using the standard mix of 1.5 % and 4.25 % dextrose monohydrate 2 litre bags, Grodstein and his colleagues [19] found that daily absorption of dextrose ranged from about 90 g when "light" and "heavy" bags were used in a ratio of 4:1 and about 300 g when "heavy" bags were used throughout the cycle. From their graphs one can calculate that the average patient using 1 or 2 heavy bags in a 24 hour cycle will absorb between 100 and 200 g per day, contributing 400 to 800 kilocalories, with an appreciable scatter between patients. Despite this continuous transperitoneal infusion of dextrose, average blood dextrose levels do not rise, and may fall, compared with undialysed uraemics [20] because CAPD partially corrects glucose intolerance by abolishing peripheral insulin resistance [21].

Nonetheless the dextrose absorption has important metabolic consequences. It suppresses appetite and may lead to a decreased intake of other important nutrients such as protein. Despite this effect many patients gain weight predominantly due to increased body fat; the median weight gain in the Newcastle series was between 5 and 10 % of body weight but a few patients developed gross obesity [5]. Dextrose absorption is accompanied by, and is probably (at least in part) responsible for, a series of metabolic and hormonal changes [20-22]. Serum insulin is raised and serum pro-insulin and C-peptide grossly elevated; this is only partly explained by reduced metabolic clearance in renal failure and probably reflects continuous stimulation of beta-cells by dextrose infusion. Plasma glucagon is elevated throughout the 24 hours, norcturnal secretion of growth hormone is suppressed and plasma cortisol raised [20].

Protein metabolism

The peritoneal membrane is more permeable to protein than that of the haemodialyser. Peritoneal clearance is determined by molecular weight [23] but with a much higher level for size-restriction or "cutt-off" than in even the most permeable HD membranes. Patients on CAPD lose on average just under 10 g of protein per day [24, 25], rising to at least twice this figure during episodes of peritonitis. The loss of albumin is well into the "nephrotic range" but CAPD patients maintain serum total protein and albumin levels in the lower normal range [5] presumably because they do not have an additional burden of protein breakdown during tubular reabsorption that affects the patient with nephrotic syndrome. With a protein intake of 1.4 g per kg per day, they can maintain normal nitrogen balance and they adapt to substantially lower protein intakes [26]. Losses of amino acids contribute a modest additional burden equivalent to 3 grams of protein a day [27].

Because of the continuous protein leak and the extra burden of peritonitis, nutritional monitoring of patients is advisable. It has shown a substantial incidence of protein-caloric malnutrition, as judged by criteria such as muscle mass, in both CAPD and HD patients [28]. This is partly a legacy of the uraemic state before dialysis but it does not always improve on CAPD.

Lipid Metabolism

Patients in end stage renal failure manifest changes in their plasma lipid pattern which are thought to be atherogenic — raised total, LDL and VLDL cholesterol, reduced HDL cholesterol, and hypertriglyceridaemia; there are corresponding changes in the Apolipoproteins (lowered ApoA-I, ApoA-II, and Apo-E, normal levels of Apo-B and ApoC-1 and increased levels of ApoC-II and

particularly ApoC-III) which correlate with the presence or absence of atheroma [29]. During the first year of CAPD these changes worsen, with a rise in serum triglycerides and in total, LDL and VLDL cholesterol and little change in HDL cholesterol [30]; the changes stabilise after about 1 year. Even patients with a normal serum cholesterol in renal failure may have profound abnormalities in lipid metabolism; HD patients and, to a lesser extent, CAPD patients have a reduced transport of cholesterol from cells to plasma which probably plays a part in their atheroma since it is found in other hyperlipidaemias which lead to arterial disease [31]. So far clinical observations do not substantiate the hope that CAPD patients, having a lesser abnormality in cholesterol transport than HD patients, will suffer less from atheroma.

As in other hyperlipidaemias, the abnormalities can be reduced by attention to diet — reducing the proportion of calories obtained from total fat and particularly saturated fat. This probably accounts for the lower prevalence of lipid abnormalities in CAPD patients eating a Chinese diet [32]. Supplements of fish oil, which are enjoying a vogue for the management of all hyperlipidaemias, reduce the hypertriglyceride level in CAPD patients but there are contradictory reports of their effect on plasma cholesterol and its subfractions [33, 34].

Alternative osmotic agents

Glucose in the dialysis fluid probably plays a part in the abnormalities of carbohydrate metabolism and the associated hormonal changes, lipid metabolism and, by depressing appetite, protein metabolism; it certainly contributes to obesity. The search is on for alternative osmotic agents which have fewer side effects. The first to be used clinically was a mixture of amino acids, designed to replace protein losses, restore normal plasma amino acids profile and act as an osmotic agent. Oreopoulos and his colleagues [35] showed that a 2 % amino acids solution had very similar osmotic activity to 1.5 % glucose monohydrate and that about 90 % of the amino acids were absorbed during a 6 hour dwell. Recent studies have confirmed these results and shown that by raising the branch-chain amino acid content of the solution one can restore plasma amino acid profile to a more normal pattern at least during the duration of a 6 hour dwell [36]. The prospect of a 24 hour cycle during which one bag of four contained amino acids is an attractive one but the solutions are expensive and extended observation of their metabolic effects will have to await a more plentiful commercial source.

Glycerol seemed on theoretical grounds a sensible alternative to glucose. Weight for weight it exerts a stronger osmotic attraction and it is readily metabolised. However it proved disappointing. It was rapidly absorbed through the peritoneum so that its osmotic effect was lost early in the cycle and plasma glycerol rose to levels 8-80 times normal when "light" and "heavy" bags designed to match the osmotic force of their glucose equivalents. The greatest attraction of the glycerol solutions is in the treatment of diabetics; in studies extending over 18 months such patients adapted well to glycerol and the "light" bags with 1.4 % glycerol produced very acceptable plasma glycerol levels with plasma osmolality in the lower "uraemic range"; even with "heavy bags" containing 2.5 % glycerol plasma osmolality was maintained at around 325 mmosl/l which was well tolerated, apart from one episode of hyperosmolar coma for which the hyperglycerolaemia was partly responsible [38]. Hypertriglyceridaemia increased during treatment even when artefacts of measurement were eliminated. The eventual place of glycerol as an osmotic agent has yet to be determined.

Polyelectrolyte solutions were introduced in the hope that their harge would delay peritoneal absorption and prolong their osmotic effect. Recent studies [39] show that the charge has little effect and that the solutions act largely as macromolecules. Daniles and his colleagues [39] concluded that neutral macromolecules should be investigated as osmotic agents. One such molecule is already undergoing clinical trials [40]; a glucose polymer solution with a mean molecular weight of 16,800 daltons has proved an effective osmotic agent because its lower osmotic pull is balanced by its slower peritoneal absorption. Fewer calories are taken up by the patient and the solution is well tolerated. The complication to date is a rise in plasma maltose which perists for some hours. An equilibration level will no doubt be reached as maltose is removed by CAPD bur further study of this problem will be required before glucose polymer can be recommended, initially as an agent for the overnight dwell. No doubt you will hear more of this topic from Dr Gokal.

References

1. Heaton A, Rodger RSC, Sellars L, Goodship THJ, Fletcher K, Nikolakakis N, Ward MK, Wilkinson R and Kerr DNS: Continuous peritoneal dialysis after the honeymoon; review of experience in Newcastle 1979-1984. *Brit Med J* 293:938-941, 1986.
2. Gokal R, Jacubowski C, King J, Hunt L, Bogle S, Baillod R, Marsh F, Ogg C, Oliver D, Ward M and Wilkinson R: Outcome in patients on continuous ambulatory peritoneal dialysis and haemodialysis; 4 years analysis of a prospective multicentre study. *Lancet* ii:1105-1109, 1987.
3. Donnelly PK, Lennard TWJ, Proud G, Taylor RMR, Henderson R, Fletcher K, Elliott R, Ward MK and Wilkinson R: Continuous ambulatory peritoneal dialysis and renal transplantation; a five year experience. *Brit Med J* 291:1001-1004, 1985.

4. Evangelista JB, Bennett-Jones D, Cameron JS, Ogg C, Williams DG, Taube DH, Neild G and Rudge C: Renal transplantation in patients treated with haemodialysis and short term and long term continuous ambulatory peritoneal dialysis. *Brit Med J* 291:1004-1007.
5. Ramos JM, Gokal R, Siamopolous K, Ward MK, Wilkinson R and Kerr DNS: Continuous ambulatory peritoneal dialysis: three years' experience. *Q J Med* 52:165-186, 1983.
6. Sandle GI, Gaiger E, Tapster S and Goodship THJ: Evidence for large intestinal control of potassium homeostasis in uraemic patients undergoing long-term dialysis. *Clin Sci* 73:247-252, 1987.
7. Martin RS, Panese S, Virginillo M, Giménez M, Litardo M, Arrizurieta E and Hayslett JP: Increased secretion of potassium in the rectum of humans with chornic renal failure. *Am J Kidney Dis* 8:105-110, 1986.
8. Panese S, Martin RS, Virginillo M, Litardo M, Siga E, Arrizurieta E and Hayslett JP: Mechanism of enhanced transcellular potassium-secretion in man with chronic renal failure. *Kidney Int* 31:1377-1382, 1987.
9. Nissenson AR: Acid-base homeostasis in peritoneal dialysis patients. *Int J Artif Organs* 7:175-176, 1984.
10. Bazzato G, Coli U, Landini S, Fracasso A, Morachiello P, Righetto F and Scanferla F: Xylitol and low dosages of insulin: new perspectives for diabetic uremic patients on CAPD. *Peritoneal Dialysis Bulletin* 2:161-164, 1982.
11. Brautbar N and Gruber HE: Magnesium and Bone Disease. *Nephron* 44:1-7, 1986.
12. Fleming LW, Lenman JAR and Stewart WK: Effect of magnesium on nerve conduction velocity during regular dialysis treatment. *J Neurol Neurosurg Psychiat* 35:342-355, 1972.
13. Mennes P, Rosenbaum R, Martin K and Slatopolsky E: Hypomagnesemia and impaired parathyroid hormone secretion in chronic renal disease. *Annals of Internal Medicine* 88:206-209, 1978.
14. Rude KR, Oldham SB, Sharp CF and Singer RF: Parathyroid hormone secretion in magnesium deficiency. *Clin Endocrinol Metab* 47:800-806, 1978.
15. Gokal R, Ramos JM, Ellis HA, Parkinson I, Sweetman V, Dewar J, Ward MK and Kerr DNS: Histological renal osteodystrophy, and 25 hydroxycholecalciferol and aluminium levels in patients on continuous ambulatory peritoneal dialysis. *Kidney Int* 23:15-21, 1983.
16. Channon SM, Osman OM, Boddy I, Rodger RCS, Goodship THG, Smith PA, Wilkinson R and Ward MK: Serum aluminium measurement: a false sense of security? In *Aluminium and other trace elements in renal disease.* Edited by Taulor A, published by TransMedica Europe Ltd 1986, 171-177, 1986.
17. De Francisco AM, Ellis HA, Owen JP, Cassidy MJD, Farndon JR, Ward MK and Kerr DNS: Parathyroidectomy in chronic renal failure. *Quart J Med* 55:289-315, 1985.
18. Cassidy MJD, Owen PJ, Ellis HA, Dewar J, Robinson CJ, Wilkinson R, Ward MK and Kerr DNS: Renal osteodystrophy and metastatic calcification in long-term continuous ambulatory peritoneal dialysis. *Quart J Med* 54:29-48, 1985.
19. Grodstein GP, Blumencrantz MJ, Kopple JD, Moran JK and Coburn JW: Glucose absorption during continuous ambulatory peritoneal dialysis. *Kidney Int* 19:564-567, 1981.
20. Heaton A, Johnston DG, Haigh JW, Ward MK, Alberti KGMM and Kerr DNS: Twenty-four hour hormonal and metabolic profiles in uraemic patients before and during treatment with continuous ambulatory peritoneal dialysis. *Clin Sci* 69:449-457, 1985.
21. Heaton A, Taylor R, Johnston DG, Gray P, Ward MK, Wilkinson R and Alberti KGMM: Hepatic and peripheral insulin action in chronic renal failure before and during continuous ambulatory peritoneal dialysis. 1988. Submitted to *Clinical Science.*
22. Wideröe T-E, Smeby LC and Myking OL: Plasma concentration and transperitoneal transport of native insulin and C-peptide in patients on continuous ambulatory peritoneal dialysis. *Kidney Int* 25:82-87, 1984.
23. Krediet RT, Zuyderhoudt FMJ, Boeschoten EW and Arisz L: Perioneal permeability to proteins in diabetic and non-diabetic continuous ambulatory peritoneal dialysis patients. *Nephron* 42:133-140, 1986.
24. Blumenkrantz MJ, Gahl GM, Kopple JD, Kamdar AV, Jones MR, Kessel M and Coburn JW: Protein losses during peritoneal dialysis. *Kidney Int* 19:593-602, 1981.
25. Kaysen GA and Schoenfeld PY: Albumin homeostasis in patients undergoind continuous ambulatory peritoneal dialysis. *Kidney Int* 25:107-114, 1984.
26. Blumenkrantz MJ, Kopple JD, Moran JK and Coburn JW: Metabolic balance studies and dietary protein requirements in patients undergoing continuous ambulatory peritoneal dialysis. *Kidney Int* 21:849-861, 1982.
27. Kopple JD, Blumenkrantz MJ, Jones MR, Moran JK and Coburn JW: Plasma amino acid levels and amino acid losses during continuous ambulatory peritoneal dialysis. *Am J Clin Nutr* 36:395-402, 1982.
28. Marckmann P: Nutritional status of patients on hemodialysis and peritoneal dialysis. *Clin Nephrol* 29:75-78, 1988.
29. Attman P-O, Alaupovic P and Gustafson A: Serum apolipoprotein profile of patients with chronic renal failure. *Kidney Int* 32:368-375, 1987.
30. Ramos JM, Heaton A, McGurk JG, Ward MK and Kerr DNS: Sequential changes in serum lipids and their subfractions in patients receiving continuous ambulatory peritoneal dialysis. *Nephron* 35:20-23, 1983.
31. Dieplinger H, Schoenfeld PY and Fielding CJ: Plasma cholesterol metabolism in end-stage renal disease. Difference between treatment by haemodialysis or peritoneal dialysis. *J Clin Invest* 77:1071-1083, 1986.
32. Chan MK and Yeung CK: Lipid metabolism in 31 Chinese patients on three 2-L exchanges of CAPD. *Peritoneal Dialysis Bulletin* 6:12-16, 1986.
33. Acker BAC van, Bilo HJG, Popp-Snijders C, Bronswijk H van, Oe PL and Donker AJM: The effect of fish oil on lipid profile and viscosity of erythrocyte suspensions in CAPD patients. *Nephrol Dial Transplant* 2:557-561, 1987.
34. Lempert KD, Rogers JS and Albrink MJ: Effects of dietary fish oil on serum lipids and blood coagulation in peritoneal dialysis patients. *Am J Kidney Dis* 11:170-175, 1988.
35. Oreopoulos DG, Marliss E, Anderson GH, Dombros N, Williams P, Khanna R, Rodella H and Brandes L: Nutritional aspects of CAPD and the potential use of amino acid contajning dialysis solutions. *Peritoneal Dialysis Bulletin* 3 (supplement 1):S10-S12, 1983.
36. Gooship THJ, Lloyd S, McKenzie PW, Earnshaw M, Smeaton I, Bartlett K, Ward MK and Wilkinson R: Short-term studies on the use of amino acids as an osmotic agent in continuous ambulatory peritoneal dialysis. *Clin Sci* 73:471-478, 1987.
37. Heaton A, Ward MK, Johnston DG, Nicholson DV, Alberti KGMM and Kerr DNS: Short-term studies on the use of glycerol as an osmotic agent in continuous ambulatory peritoneal dialysis. *Clin Sci* 67:121-130, 1984.
38. Matthys E, Dolkart R and Lameire N: Extend use of a glycerol-containing dialysate in diabetic CAPD patients. *Peritoneal Dialysis Bulletin* 7:10-15, 1987.
39. Daniels FH, Nedev ND, Cataldo T, Leonard EF and Cortell S: The use of polyelectrolytes as osmotic agents for peritoneal dialysis. *Kidney Int* 33:925-929, 1988.
40. Mistry CD, Mallick NP and Gokal R: Ultrafiltration with an isosmotic solution during long peritoneal dialysis exchanges. *Lancet* 2:178-182, 1987.