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Peritoneal dialysis in children

Review of 8 years' experience

RUTH E. DAY AND R. H. R. WHITE

From the Children's Hospital, Birmingham

SUMMARY During the years 1968–75, 59 periods of peritoneal dialysis were performed on 44 children aged from 2 days to 17 years. The commonest complication was peritoneal infection, which affected 68% of those under 2 years and 30% of older children. This was satisfactorily treated in all but one case which was due to *Candida albicans*. The use of combined intramuscular and intraperitoneal gentamicin therapy is described. 2 patients died as a result of massive intraperitoneal haemorrhage and one had a nonfatal intestinal perforation. In experienced hands peritoneal dialysis is a convenient, effective, and reasonably safe way of treating acute renal failure; it is best performed in centres capable of handling complex metabolic problems and investigating and treating the underlying renal disease.

Because peritoneal dialysis (PD) is simpler, less costly, and more readily available than haemodialysis, it is the method of choice for children with acute renal failure who are deteriorating despite careful conservative management (Meadow *et al.*, 1970). It may be also used in conjunction with dietary protein restriction and calorie supplementation in patients with chronic renal failure, while undergoing diagnostic investigation or awaiting haemodialysis or transplantation (Leigh, 1969). Several authors (Thomson *et al.*, 1964; Ribot *et al.*, 1966; Stewart *et al.*, 1966; Leigh, 1969) have described the problems of PD in adults, the main one being infection. Meadow *et al.* (1971) described their experience of PD in 11 children but did not comment on complications. Segar *et al.* (1961), Etteldorf *et al.* (1962), Gianantonio *et al.* (1962), and Lloyd-Still and Atwell (1966) reported small numbers of children dialysed mostly for less than 48 hours. In this paper we review the reasons for using PD and its results in children during the past 8 years, and draw particular attention to the commonest complication, infection.

Technique

The child is sedated if necessary. All attendants wear face-masks and the operator sterile gown and gloves. The site chosen for insertion of the catheter is in the midline, approximately one-third of the distance from the umbilicus to the pubic symphysis. After skin preparation with 0·5% chlorhexidine in spirit, the abdominal wall is infiltrated with 1% lignocaine, and 100–300 ml dialysing fluid is then run into the peritoneal cavity through a no. 1 gauge needle. A single McGaw Laboratories' catheter is inserted through a stab incision, with the aid of the trocar supplied. In older children the tip of the catheter is directed towards the pelvis but in infants the left or right paracolic gutter is preferred because of the shallowness of the pelvis. The paediatric catheter is found suitable for infants and most children up to 6 years old, after which the adult size is usually used. The catheter is held in place by a purse-string suture and the surrounding skin painted with 1% gentian violet tincture before applying a waterproof dressing, which is changed as necessary. The protruding portion of the catheter is trimmed to about 5 cm. Recently we adopted a simple technique to protect it from the weight of clothes (Comley, 1976); a presterilized, disposable 100 ml polyethylene gallipot is inverted over the catheter, which is threaded through a perforation made in its base before trimming.

The catheter is joined via a right-angle connector to the giving-set, which consists of delivery, drainage, and terminal lines interconnected by a Y-piece as a sealed unit. Prewarmed dialysis solution is delivered by gravity, and drainage is effected by siphoning into a sealed bag suspended beneath the bed. Heparin 500 units is added to each litre of dialysing fluid. Initially we also added penicillin but

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discontinued this in 1969 when a child requiring dialysis developed *Candida* peritonitis. Cycles of 25–30 ml/kg body weight are generally used, with care to avoid embarrassing respiration in infants or causing severe discomfort in older children. The first cycle is drained immediately, in order to confirm patency of the system.

Our practice in treating *acute renal failure* is to give continuous PD until the blood urea level falls to approximately 17 mmol/l (102 mg/100 ml), and then to dialyse by daytime only, until a diuresis ensues. For the purpose of analysis we have defined this as a single 'period' of PD. In order to minimize the risk of infection the giving-set is changed every 48 hours during continuous PD, and daily during intermittent dialysis. The attendant nurse washes and dries her hands but it has not been customary to wear either mask or gloves. During intermittent PD the cannula is spigotted overnight. On completion of the period of dialysis the cannula is removed; otherwise it is only removed in the event of blockage, etc. In a small number of patients with *chronic renal failure* each weekly period of dialysis lasted approximately 2 days, after which the cannula was removed, and reinserted the following week through a new incision. In all cases 5–10 ml dialysate was aspirated daily for culture by syringe and needle from the injection port on the right-angle connector.

Results

All patients who underwent PD in this hospital during the years 1968–75 inclusive were reviewed. There were 24 boys and 20 girls aged 2 days to 17 years. The reasons for dialysis and the outcome are given in Table 1. 10 patients were known to have chronic renal failure and 5 had a diagnosis of rapidly progressive glomerulonephritis confirmed on renal biopsy, after initial dialysis. The remaining 29 children were presumed at the time of treatment to have potentially reversible acute renal failure. The haemolytic-uraemic syndrome (HUS) was the commonest cause, accounting for 56% of children with acute renal failure and 43% of the total number dialysed. 59 periods of dialysis, ranging in duration from 1 to 25 days, were performed on the 44 patients, 2 children with HUS and 6 with chronic renal failure undergoing dialysis more than once each.

Serious complications. 22 (50%) of the 44 patients died. Though in 13 instances this occurred within 2 weeks of dialysis, only 5 deaths could be wholly or partly attributed to it. A 9-year-old girl developed *Candida* peritonitis which did not respond to therapy with amphotericin B, but was also suffering from rapidly progressive glomerulonephritis. A 2-year-old girl with HUS, who had been treated with streptokinase, died suddenly 16 hours after discontinuation of PD; necropsy examination showed massive intraperitoneal haemorrhage (Stuart *et al.*, 1974). An infant with bilateral renal venous thrombosis had a massive intraperitoneal haemorrhage with shock at the time of insertion of the catheter and, though he was resuscitated with plasma and blood, he died as a result of severe cerebral hypoxia. At necropsy it appeared that the haemorrhage had originated retroperitoneally owing to accidental perforation of a blood vessel, presumably by the trocar during its insertion. Both kidneys showed extensive venous infarction.

Two children with chronic renal failure collapsed and died during or just after dialysis; one was known to be hypertensive and showed cerebral oedema with coning of the uncus at necropsy. The other child, who had received prolonged calciferol therapy for osteodystrophy, was found at necropsy to have extensive metastatic calcification and myocardial fibrosis. Another major but nonfatal complication arose in an infant with renal venous thrombosis. An adult catheter was inadvisedly used and had been shortened by cutting the perforated distal end before insertion. This caused a local area of necrosis in the ileum, with perforation necessitating laparotomy.

Table 1 *Diagnosis, age at dialysis, and outcome*

Diagnosis	*Total no.*	*Age at dialysis*		*Outcome*	
		<2 yr	*≥2 yr*	*Survived*	*Died*
Haemolytic-uraemic syndrome	19	11	8	13	6
Renal venous thrombosis	3	3		1	2
Hypernatraemic dehydration with DIC*	3	3		1	2
Extensive burns	1		1	1	
Acute renal failure—cause undetermined	2	1	1	2	
Acute poststreptococcal glomerulonephritis	1		1	1	
Rapidly progressive glomerulonephritis	5		5		5
Chronic renal failure	10		10	3	7
Total	44	18	26	22	22

*DIC, disseminated intravascular coagulation.

Table 2 *Incidence of infection related to age and duration of peritoneal dialysis (PD)*

	No. of PD periods			*Duration of PD periods (days)*	
Age (yr)	*Total*	*Infected*	(%)	*Range*	*Mean*
<2	19	13	(68)	2–16	8
⩾2	40	12	(30)	2–25	7
Total	59	25	(42)	2–25	7·3

Protein loss. The protein concentration of the dialysate was measured in 95 daily collections from 15 patients and ranged from 0·1–5·0 g/l. The daily protein loss ranged from 0·06–4·4 g/kg body weight, with a mean of 0·58 g/kg. However, daily losses greater than 2·0 g/kg were observed in only 2 patients, on both occasions during the first day of dialysis.

Infection. The commonest complication was intraperitoneal infection, which was diagnosed in 25 PD periods (42%). The diagnosis of infection requires some explanation. A positive dialysate culture may sometimes be the result of contaminants; moreover, neutrophils may be present in the absence of infection owing to chemical irritation, and turbidity as the result of high protein content of the dialysate (Wardle, 1973). In our series we did not diagnose infection if symptoms were absent and dialysate culture yielded only a scanty growth of organisms, or leucocytes were found in sterile fluid. In 5 instances where culture gave a moderate or heavy growth, however, infection was diagnosed and treated despite the lack of symptoms. In the remaining 20 infected PD periods, positive culture was associated with symptoms; 16 had fever, 3 rigors, and 8 either abdominal pain, diarrhoea, or vomiting. The Fig. shows that there is a relationship between the incidence of infection and the duration of PD; all patients dialysed for more than 11 days became infected. The incidence of infection was considerably higher in children under 2 years old than in older children (Table 2), even though the mean duration of PD in both age groups was similar. No child died solely as a result of peritonitis, though *Candida albicans* infection undoubtedly contributed to death in a child with rapidly progressive glomerulonephritis.

The organisms cultured from the peritoneal dialysate are shown in Table 3. In 17 instances a single organism was isolated, but in 8 patients mixed cultures were obtained or different organisms isolated on 2 occasions. Blood cultures yielded *Staphylococcus pyogenes* and a coliform in one case each, but were sterile in the remaining 15 instances. Antibiotic sensitivities were determined for 30 out of the 35 organisms cultured. Most staphylococci and Gram-negative organisms were insensitive to ampicillin

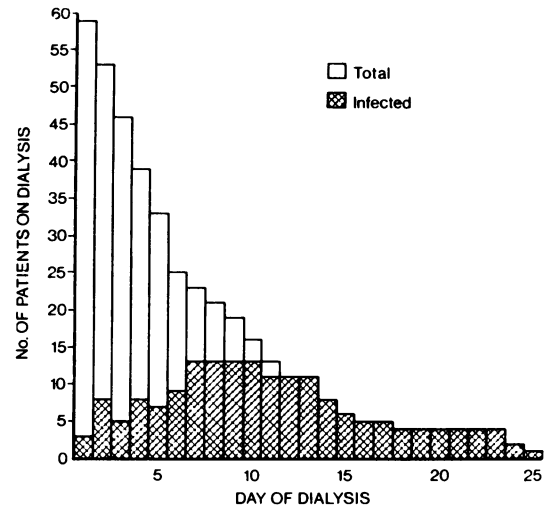

Fig. *Incidence of peritoneal infection related to duration of dialysis.*

and the latter to sulphonamides also, but all bacteria tested (streptococci not being included) were sensitive to gentamicin, which was used successfully as treatment in 14 children.

During the past 2 years we have used the technique described by Smithivas *et al.* (1971), in which a single loading dose of gentamicin is given intramuscularly or intravenously, followed by continuous

Table 3 *Micro-organisms cultured from dialysate*

Micro-organism	*Total no.*	*Age of child*	
		<2 yr	*⩾2 yr*
Esch. coli	13	8	5
Klebsiella spp.	1	1	
Serratia marcescens	1		1
Proteus spp.	1	1	
Pseudomonas aeruginosa	2	1	1
Flavobacterium spp.	1		1
Staphylococcus pyogenes	6	3	3
Coagulase-negative staphylococci	3	2	1
Streptococcus viridans	1		1
Streptococcus faecalis	1		1
Candida albicans	5	2	3
Total	35	18	17

intraperitoneal administration. In order to gain more information about the correct dosage, serial assays of serum levels of gentamicin were carried out in 4 children undergoing this treatment, using the plate diffusion method. They were given an initial dose of 2 mg/kg IM in one and IV in three instances, and gentamicin was then added to the dialysis fluid at a concentration ranging from 3 to 12·5 μg/ml, the aim being to achieve a serum level of 3–7 μg/ml. The dialysis fluid concentrations administered and the serum levels which they yielded are given in Table 4. Cases 1, 2, and 4 had peritoneal infection, while Case 3 was being treated prophylactically for extensive burns. The relatively low serum : dialysis-fluid ratios observed in Case 3 and in Case 2 on day 7, despite increasing dialysis fluid concentrations, might be explained by the slower diffusion of the drug in the absence of peritoneal inflammation.

Candida albicans was isolated from dialysate in 5 patients. In 2 children dialysis was discontinued and the catheter removed before reports of positive culture were received; in the absence of clinical evidence of infection, treatment was withheld, and neither child developed peritonitis subsequently. 2 further children were given amphotericin B intraperitoneally. In a 9-year-old girl with rapidly progressive glomerulonephritis the drug was given continuously at a concentration of 5μg/ml in the dialysis fluid and, though at necropsy there appeared to be peritonitis, culture and histology showed no evidence of *Candida*. In a 14-year-old boy with polyarteritis nodosa a single dose of 50 μg amphotericin B was instilled into the peritoneal cavity before PD was discontinued; though during subsequent PD *Candida* was not cultured, it was shown by histological examination post mortem. The fifth child, whose dialysate on the last day of dialysis contained visible floccules of mycelium and gave a pure, heavy growth of *Candida* on culture, was treated with a single intraperitoneal injection of 100 mg 5-fluorocytosine, followed by removal of the catheter, and recovered without developing symptomatic peritonitis.

Discussion

In this series infection was the main complication of PD, affecting 42% of patients. The reasons for this are worth examining. Firstly, the duration of dialysis appears to be an important factor; all those dialysed for more than 11 days became infected. Stewart *et al.* (1966) reported an infection rate in adults of 10% before and 33% after 4 days' dialysis. Leigh (1969) experienced no infection before the third day; the infection rate rose to 26% in the first week and then fell. In the previously reported series in children (Segar *et al.*, 1961; Etteldorf *et al.*, 1962; Giantonio *et al.*, 1962; Lloyd-Still and Atwell, 1966) the majority had been dialysed for less than 48 hours; of those dialysed for longer 3 out of 5 became infected.

Secondly, uraemia itself interferes with immune responses and neutrophil function (Boulton-Jones *et al.*, 1973). Moreover, some of our patients with rapidly progressive glomerulonephritis were receiving corticosteroids and cytotoxic agents, while those with HUS were severely anaemic. These factors would probably combine to reduce the resistance to infection.

Thirdly, Leigh (1969) showed that an organism identical with that causing the peritonitis could be isolated from the nose, skin, and faeces in 46% of cases and concluded that the major source of infection was the skin around the dialysis catheter. In very young children, who are incontinent of faeces, colonization of the skin around the site of insertion of the catheter by faecal organisms must presumably increase the risk of infection. This is supported by the observations that the incidence of peritoneal infection in children under 2 years old is increased (Table

Table 4 *Gentamicin concentrations (μg/ml) administered in dialysis fluid (D) and those obtained as a result in the serum (S).*

Case no.	*Organism isolated*	*Day of dialysis*									
		1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*
1	*Staph.*										
	D	3·0		3·0							
	S	4·0		3·5							
2	*Esch. coli*										
	D	5·0	5·0		5·0	10·00		10·0			
	S		3·9		3·0			4·2			
3	None isolated										
	D	5·0	7·5	10·0		12·0	12·0		5·0		5·0
	S	2·5	2·5	3·3			6·0				2·4
4	*Esch. coli*										
	D	5·0		5·0	6·0			6·0			
	S			2·8				4·8			

2), and that 11 out of 19 dialysis periods (58%) in the younger age group were complicated by infection with faecal organisms, compared with only 9 out of 40 (23%) in older children.

As we made no major changes in our methods during the period of study, we are unable to comment usefully on the significance of such factors as the frequency of renewing the giving-set and cannula, and aseptic technique. However, the direct relationship between the duration of PD and the development of infection, together with the observed frequency of enterobacterial infections in younger children, are consistent with the belief that organisms colonizing the skin of the abdominal wall gain access to the peritoneal cavity via the cannula track. This risk, if real, could be minimized by removing the cannula at, say, 48-hour intervals and reinserting it through a new incision. However, it is somewhat doubtful whether the benefits of such meticulous technique would outweigh the psychological disadvantages, and our preference is for careful monitoring of infection and prompt treatment when it is diagnosed.

Smithivas *et al.* (1971) showed that gentamicin given intramuscularly yielded low dialysate levels and unpredictable blood concentrations, whereas if given in the dialysis fluid it produced serum levels approaching those in the dialysate within 12 hours. They reported gentamicin as being a useful single drug for the initial treatment of bacterial peritonitis, pending the results of dialysate culture, but suggested adding carbenicillin if *Pseudomonas* was isolated, and substituting a penicillin or cephalosporin if staphylococci were found. From our experience we doubt whether this is necessary unless the clinical response is unsatisfactory or streptococci are isolated. To be effective gentamicin must reach adequate serum levels and yet, if given in excess, it is toxic. Jackson and Arcieri (1971) found evidence of ototoxicity in 2% of patients treated with gentamicin and concluded that toxicity was related to high serum concentrations. Peak levels above 12 μg/ml have been suggested as toxic but Jackson and Arcieri (1971) concluded that sustained, moderately high levels might be equally damaging. More recently Mawer *et al.* (1974) observed a better correlation with the 'baseline area' which is the mean trough level in the serum multiplied by the duration of treatment in days. They found that 4 out of 5 patients with baseline areas >45 μg-days/ml developed ototoxicity.

Barber and Waterworth (1966) reported *in vitro* studies which showed that the minimum inhibitory concentration of gentamicin for all strains of staphylococci and *Esch. coli* tested, and for most strains of *Ps.pyocyanea* and *Proteus*, was 4 μg/ml or less. Thus, for treatment of peritoneal infection it seems reasonable to aim for a serum concentration of 4–5 μg/ml and to continue therapy for no longer than 10 days. On the basis of the data which we have presented, we would suggest a parenteral loading dose of 2 mg/kg, followed by an initial concentration of 5 μg/ml in the dialysis fluid. The latter should be adjusted according to serum levels and a higher concentration may well be necessary in the absence of peritonitis.

Holdsworth *et al.* (1975) reported successfully treating *Candida* peritonitis with 5-fluorocytosine (5-FC) in an adult patient receiving maintenance PD for chronic renal failure. They found that by adding 5-FC to the dialysis fluid at a concentration of 50 μg/ml they could achieve a constant, effective, and nontoxic blood level which could be varied as necessary despite renal functional impairment, in addition to maximum concentration of the drug at the site of infection. Compared with amphotericin B, 5-FC has the advantage that it can be given orally if necessary after discontinuation of PD (Phillips *et al.*, 1973), and is also less toxic. Its use in the treatment of *Candida* peritonitis complicating PD should be futher explored.

Dialysate protein loss is not so much a complication as an unavoidable disadvantage of PD. Berlyne *et al.* (1967) measured the protein content of dialysate in 12 adults and found a range of 10·5–44 g/day. They found all plasma protein constituents present but the albumin/globulin ratio was higher than in plasma. In our patients the mean daily protein loss was 0·58 g/kg, equivalent to approximately 17 g/day in a 30 kg child. This loss should be taken into account when the dietary protein requirements are being considered; indeed the opportunity to give additional protein should be seized while the patient is on dialysis.

Bleeding into the peritoneal cavity is usually minimal or absent. We observed that the dialysate was often uniformly bloodstained when we used undiluted dialysis solution with dextrose content of ⩾6·3%, and nowadays use this diluted with an equal volume of solution containing 1·5% dextrose. For this reason we believe that a preparation containing 4% dextrose would be more suitable for paediatric use where hypertonic fluid is indicated.

Serious technical complications are fortunately rare. Phillips *et al.* (1973) reported perforation of the transverse colon in an adult patient during insertion of the catheter, with survival after laparotomy. Massive and fatal haemorrhage occurred in 2 very young children in this series. From Table 1 it is apparent that a high proportion of children requiring dialysis will have an increased bleeding tendency owing to consumption coagulopathy, enhanced by anticoagulant or thrombolytic therapy in some

instances. Because of the short distance separating the anterior and posterior abdominal walls in young children, the risk of traumatizing blood vessels on inserting the trocar and catheter is increased. This can, however, be minimized by running 100–200 ml dialysis fluid into the peritoneal cavity and by incising the full thickness of the abdominal wall with a no. 15 scalpel blade before inserting the trocar and catheter.

Thus, PD can be regarded as a simple, effective, and reasonably safe method of treating children with acute renal failure for whom conservative management has proved insufficient. However, the dialysis itself is perhaps the simplest aspect of the overall management of acute renal failure. As Meadow *et al.* (1970, 1971) have emphasized, such children may be exceedingly ill and present complex fluid and electrolyte problems, may often require special diagnostic facilities available only in a limited number of centres, and may prove to have, or later develop, underlying chronic renal disease necessitating haemodialysis or transplantation. Moreover, the needs for PD in children are small compared with adults. From the Fig. it can be calculated that during the 8 years under consideration there were 420 dialysis days—an average of 52·5 days per annum, in a regional centre serving more than 5 million people. The average district hospital paediatric department is therefore unlikely to acquire extensive experience. For these reasons we believe that optimum results are more likely to be achieved in centres specializing in the investigation and treatment of children with renal disease.

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Correspondence to Dr. R. H. R. White, Children's Hospital, Ladywood Middleway, Birmingham B16 8ET.