

PERITONITIS COMPLICATING ACUTE PERITONEAL DIALYSIS IN NORTHEAST MALAYSIA

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Abstract. A prospective observational study examining the incidence, predisposing factors and microbiological aspects of peritonitis complicating acute intermittent peritoneal dialysis (IPD) was performed in Hospital Universiti Sains Malaysia, a referral hospital situated in Northeast Malaysia. Over a 7- month period, a total of 126 acute IPD treatments were included involving 69 patients. The majority of patients suffered from chronic or end stage renal failure (92.7%) and nearly half (47.8%) have underlying diabetes mellitus. Peritonitis occurred in 25 treatment sessions giving a frequency of 19.8% of procedures performed. The mean interval between starting dialysis and the first sign of peritonitis was 3.5 days, with 12% of peritonitis occurring before day 3 of treatment. Frequent catheter manipulation and/or leakages were identified as significant predisposing factors for peritonitis and the risk of peritonitis was increased with longer duration of IPD. Gram-negative infections were seen twice more commonly than gram-positive infections. We recommend the use of cloxacillin in combination with either an aminoglycoside or a cephalosporin as empirical antibiotic coverage until culture reports are available.

INTRODUCTION

Peritoneal dialysis is a procedure that has gained widespread acceptance in the treatment of acute and chronic renal failure because of its simplicity and advantages compared with other modes of dialytic treatment such as hemodialysis (Diaz-Buxo, 1990). This has led to the widespread use of peritoneal dialysis in the treatment of renal failure over the past four decades in many hospitals, both large and small (Spencer and Fanton, 1984). However the procedure may be associated with complications including peritonitis which causes significant morbidity. The incidence of peritonitis in IPD has been reported to be between 1% to 20% of procedures performed (Vanmonde *et al*, 1975; Roxe *et al*, 1976; Ribot *et al*, 1966; Vas, 1983; Delapenha *et al*, 1991; Valeri *et al*, 1993). Several reports have implicated staphylococcal species as the most frequent pathogen in chronic peritoneal dialysis associated with peritonitis (Spencer and Fenton, 1984; Vas 1983). However, gram-negative organisms are at least as frequent as, if not more frequent than gram-positive organisms in causing peritonitis associated with acute peritoneal dialysis (Vanmonde *et al*, 1975; Delapenha *et al*, 1991). Our institution, Hospital Universiti Sains Malaysia (HUSM) in Northeast Malaysia is a teaching hospital serving a population of 1.8 million. In our hospital IPD is the commonest mode of dialysis treatment for acute renal failure as well as the main form of treatment for the majority of end stage renal

failure patients who could not afford other forms of renal replacement therapy due to financial constraints.

We undertook a prospective observational study to provide local data on the incidence of peritonitis amongst our acute IPD patients. We also designed the study to identify the predisposing factors for the development of peritonitis as well as to determine the clinical features and microbiological aspects of peritonitis in our patient population.

METHODS

Patients and study protocol

A prospective study of all adult patients admitted to Hospital Universiti Sains Malaysia (HUSM) who underwent acute intermittent peritoneal dialysis (IPD) from September 1995 to March 1996 was performed. All adult patients (age \geq 13) who underwent at least 48 hours of IPD and were free of peritonitis at the start of treatment were included in the analysis. The following clinical details were recorded - age, sex, race, comorbid illnesses, underlying renal disease (if known) and type of renal failure. Exclusion criteria were pediatric patients, cases of acute abdomen due to other causes, perforated abdominal viscus and chronic ambulatory peritoneal dialysis (CAPD) patients.

Dialysis was performed mostly with acute catheters with the exception of one patient with

chronic indwelling double-cuff Tenckhoff catheter. Acute catheters were placed by medical personnel using a rigid trocar. The length and frequency of dialysis treatment and other parameters (eg number and type of solution and use of antibiotics) were determined by the medical officers and primary physicians. Dialysis was performed using either 1.5% or 4.25% glucose solutions with IL - exchanges per hour with 20 to 30 minutes of dwelling time (20 to 24 exchanges/day). The dialysis system used was a two-bag, Y tubing, gravity dependant, closed-drainage system with unprojected spikes.

Technical factors related to the IPD were documented, including occurrence of catheter manipulations (either related to several initial attempts at inserting PD catheter or reinsertion and catheter blockage), leakages and the timing of initial PD catheter insertion. The duration of PD (in days), number of cycles and amount of hypertonic solutions used were noted. For the cases diagnosed to have peritonitis, the day of diagnosis, presence of abdominal pain/tenderness, cloudy peritoneal fluid and fever were recorded.

Microbiology

Samples for random daily surveillance were obtained by filling a sterile screw top-tube with effluent drawn from a sampling port in the dialysis bag. These specimens were sent both for gram-staining and culture. Cell counts were performed by collecting samples in a similar fashion to that of cultures. Differential counts were performed after centrifugation and the sediment colored with Wright's stain.

Case definitions

Peritonitis was defined in one of two ways; (1) if at least two of three of the following criteria were met: (a) peritoneal signs or symptoms, (b) a peritoneal fluid effluent white blood cell count greater than 100 WBC/ μ l with > 50% polymorphonuclear leukocytes or (c) a positive peritoneal fluid effluent gram-stain or culture; (2) alternatively in the absence of other data, three or more positive peritoneal fluid effluent culture for the same organism (s). Relapsing peritonitis is defined as a second episode of peritonitis caused by the same organism occurring within 1 month following treatment of the first episode.

Statistical analysis

Clinical data were analysed using the Epi-

Info (6.02) and SPSS Window students version (6.0). A statistical package using χ^2 test, Fisher's exact test and Student's *t*-test were used where appropriate. Significance was accepted at p-value <0.05.

RESULTS

Patient demographics

Patient demographics are listed in Table 1. A total of 69 patients were treated during the 7-month study period involving 126 IPD sessions. The age range was 13 years to 86 years (mean 54 years). The underlying causes for chronic and end stage renal failure are illustrated in Fig 1.

Other causes of chronic/end stage renal failure are lupus nephritis(1), adult polycystic kidney disease(1), myeloma kidney(1) and renal cell carcinoma resulting in bilateral nephrectomy(1). Of the 5 patients with acute renal failure, 2 patients has SLE with lupus nephritis, 1 leptospirosis, 1 post-streptococcal glomerulonephritis and 1 carcinoma of the pancreas.

Table 1
Patient demographics.

Age	
Mean	54 years
Median	53 years
Range	13-86 years
Race	
Malays	61 (88.4%)
Chinese	7 (10.2%)
Indian	0 (0%)
Others	1 (1.4%)
Gender	
Male	45 (65.2%)
Female	24 (34.8%)
Type of renal failure	
Acute renal failure (ARF)	5 (7.3%)
Acute on chronic renal failure (CRF)	17 (24.6%)
End stage renal failure (ESRF)	47 (68.1%)
Comorbid diseases	
Diabetes mellitus	33 (47.8%)
Hypotension	11 (15.9%)
Cardiovascular	25 (36.2%)
Coagulopathy	8 (11.6%)
Sepsis	32 (46.4%)
Gastrointestinal bleeding	10 (14.5%)
Malignancy	4 (5.8%)

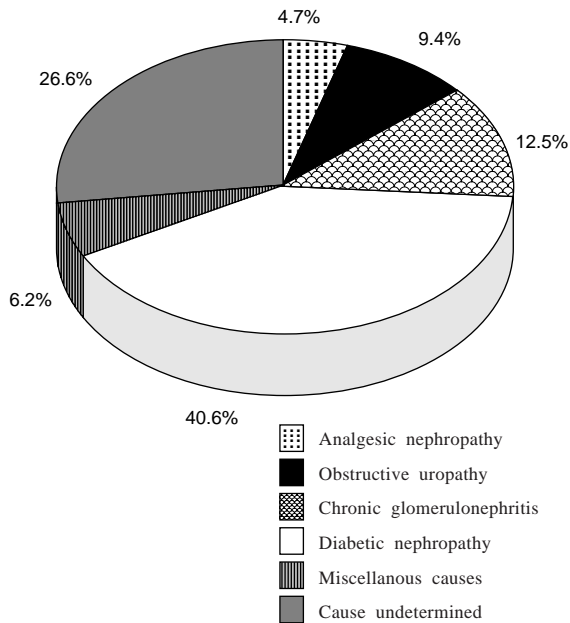


Fig 1-Causes of chronic and endstage renal failure.

IPD Demographics

Seventy-eight percent of the treatments were performed in the general ward, only 22% were performed in ICU or acute medical ward. The mean length of treatment in the general ward was 4.1 days. In ICU and acute medical ward, the mean length of treatment was 4.5 days. Overall treatment lasted for 4 days or longer in 93 IPD sessions (73.8%).

Epidemiology of peritonitis

Twenty-five cases of peritonitis were diagnosed giving a frequency of 19.8%. Peritonitis occurred twice in 4 patients. One patient had relapsing peritonitis caused by staphylococcal epidermidis. Another patient had peritonitis caused by the same organism (*E. coli*) but over a period of 2 months.

Ninety-five percent of patients who developed peritonitis suffers from chronic or endstage

Table 2
Bacteriology of peritonitis.

Organism	No.	%
Single gram-positive organisms		
<i>Staphylococcus aureus</i>	3	
<i>Staphylococcus epidermidis</i>	1	
Streptococci	1	
Multiple gram-positive organisms	1	
Total gram-positive organisms	6	24
Single gram-negative organisms		
<i>E. coli</i>	2	
<i>Pseudomonas</i>	3	
<i>Klebsiella</i>	1	
<i>Acinetobacter</i>	1	
Other single gram-negative organisms	2	
Multiple gram-negative organisms		
<i>Pseudomonas</i> + <i>Klebsiella</i>	2	
<i>E. coli</i> + <i>Klebsiella</i>	1	
<i>Pseudomonas</i> + <i>Flavobacter</i> + <i>Acinetobacter</i>	1	
“MG GNB”	2	
Total gram-negative organisms	15	60
Multiple gram-pos+gram-neg organisms		
<i>S. aureus</i> + <i>Enterobacter</i>	2	
<i>S. aureus</i> + <i>Enterobacter</i> + <i>Acinetobacter</i>	1	
<i>S. aureus</i> + <i>E. coli</i>	1	
Total mixed gram-pos+gram-neg organisms	4	16
Combined total	25	100

renal failure and 61.9% has underlying diabetes mellitus. The bacteriology of peritonitis is listed in Table 2. Twenty-four were diagnosed by criteria 1 and only 1 was diagnosed by criteria 2. Single or multiple gram-negative isolates constitutes almost two-thirds of the organisms causing peritonitis. In 2 cases of mixed growth of gram-negative bacilli "MG GNB", the individual gram-negative organisms were not identified and antibiotics sensitivity pattern not carried out. There were 3 cases of methicillin resistant *Staphylococcus aureus* (MRSA) and 2 cases of *Candida* species isolated (in combination with gram-positive organism).

The mean interval between starting dialysis and the first sign of peritonitis was 3.5 days (range 2-5 days). The diagnosis of peritonitis was made on day 2 in 12% of sessions, on day 3 in 48%, on day 4 in 20% and on day 5 in 20%. The clinical features associated with peritonitis are shown in Table 3. Fig 2 shows the frequency distribution of positive surveillance cultures and peritonitis cases over time.

In looking at possible predisposing factors for the development of peritonitis, several variable factors were compared between the IPD sessions

Table 3
Clinical features associated with peritonitis.

Sign	No. of patients	%
Abdominal pain ± tenderness	19	76
Cloudy peritoneal fluid	21	84
Fever	14	56

Table 4
Mean duration of IPD and mean number of hypertonic solutions.

Parameter	IPD with peritonitis (25)	IPD without peritonitis (101)	p-value
Mean duration of IPD (days)	4.56 (SD ± 0.961) (SEM ± 0.192)	4.009 (SD ± 0.911) (SEM ± 0.091)	< 0.05
Mean number hypertonic solutions used	11.52 (SD ± 12.53) (SEM ± 2.506)	10.32 (SD ± 13.17) (SEM ± 1.311)	> 0.05

with peritonitis and those sessions without peritonitis. The mean duration of IPD (in days) and mean number of hypertonic solutions used per session were compared between the two groups and the results shown in Table 4.

The comparisons for several other variables are listed in Table 5.

Four patients were treated with cloxacillin alone while the others were treated with a combination of cloxacillin and either an aminoglycoside (gentamicin) or cephalosporins (cefuroxime or ceftazidime) or piperacillin.

There were 5 gram - negative organisms cultured which demonstrated *in vitro* resistance to gentamicin (4) as well as to cefuroxime (1) and ceftazidime (2).

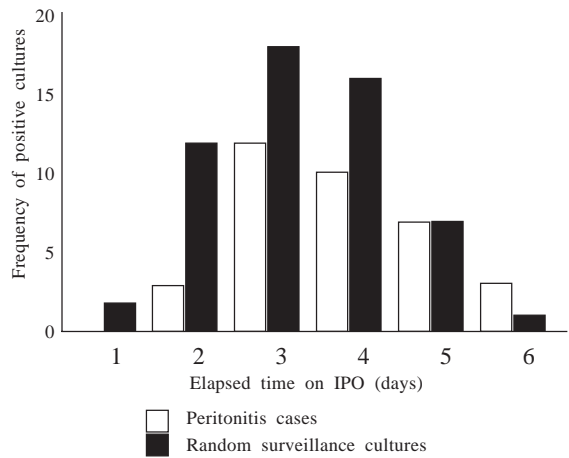


Fig 2-Frequency distribution of positive surveillance cultures and peritonitis cases over time.

Table 5
Technical variables related to IPD.

Variable	IPD with peritonitis (n=25)	IPD without peritonitis (n=101)	Relative risk (RR) Confidence interval (CI)	p-value ^a
1. Presence of catheter manipulation or leakage	16 (64%)	21 (20.8%)	4.28 (2.08-8.79)	<0.001
2. Insertion of catheter being in the evening or after midnight	10 (40%)	48 (48.0%)	0.78 (0.38-1.60)	^b NS
3. Presence of at least 2 comorbid diseases	14 (56%)	62 (61.4%)	0.84 (0.41-1.69)	^b NS

^aUsing χ^2 - test

^bNS = not significant

DISCUSSION

Acute intermittent peritoneal dialysis (IPD) is frequently used as a form of renal replacement therapy in acute as well as chronic / endstage renal failure in our hospital population. Two-third (68.1%) of our patients on acute IPD are those who have advanced to end stage renal disease. The most important limitation and perhaps the most frequent complication of this otherwise safe and effective procedure is peritonitis. This is reflected in our study where bacterial peritonitis occurred in 19.8% of all IPD sessions. Even though peritonitis is mostly a treatable complication of PD, it has been found that even after successful therapy of peritonitis, future PD may be a problem because of adhesions and compartmentalizations of fluid (Maher and Schreiner, 1965).

Peritoneal dialysis was first used for the treatment of renal failure in humans by Ganter in 1923. In 1950 a survey of the literature found that the incidence of infection was 48% amongst patients treated by continuous dialysis and was slightly less (37%) amongst those treated with intermittent dialysis. Overall it was found that peritonitis was the principal cause of death in 15% of patients (Odel *et al*, 1950). Nevertheless, the incidence of peritonitis during acute PD, which was initially as high as 50% has been reduced to more acceptable levels over the next 20 years (Vanmonde *et al*, 1975; Schwartz *et al*, 1967). The reduction in the incidence of peritonitis has been achieved by various measures, including the use of a closed drainage system, small bore catheters and limitation of dialysis to 48-72 hours (Valeri *et al*, 1993; Schwartz *et al*, 1967; Chamberlain *et al*, 1964).

In contrast to the study by Schwartz *et al* (1967) who found that none of their cases developed peritonitis before 72 hours of dialysis, a study by Valeri *et al* (1993) suggested the opposite result. Their study is probably biased because a large proportion of their patients have acute renal failure and severe intercurrent illnesses with the widespread use of antibiotics for other reasons. Our study seemed to agree with the fact that the incidence of peritonitis is increased with a longer duration of PD where only 12% of all our cases developed peritonitis before day 3 of treatment. Recent studies have reported peritonitis rates between 1 and 20% of procedures performed (Vanmonde *et al*, 1975; Roxe *et al*, 1976; Ribot *et al*, 1966; Vas, 1983; Delapenha *et al*, 1991; Valeri *et al*, 1993). In these reports however, the incidence of positive bacterial culture from the peritoneal drain ranged from 4 to 38%. In our study, although 31.7% of the surveillance cultures were positive, clinical peritonitis was seen in 19.8% of all procedures done. Such discrepancy has been noted before (Roxe *et al*, 1976; Valeri *et al*, 1993; Gjessing, 1965) and indicated the need to relate clinical status and laboratory reports. It is observed from our study that fever is only present in 56% of our patients with peritonitis. It is to be noted that a large proportion of our patients are those with CRF/ESRF where there is derangement of temperature control. Uremia per se does not appear to affect the temperature response to pyrogens. In addition the degree of interleukin - 1 (IL - 1) production by stimulated uremic monocytes is normal. However, because of baseline hypothermia (demonstrated in 50% of hemodialysis patients where the predialysis body temperature is subnormal) and possibly because of frequently coexisting

malnutrition, severe infections in some dialysis patients may not be associated with fever (Lentino and Lechey, 1994). Only 76% of our patients developed abdominal pain/tenderness. Therefore a reliable diagnosis of peritonitis then relies on the peritoneal fluid cell count (84% positive in our patients with peritonitis) as well as prompt delivery of peritoneal fluid specimen to the laboratory for culture.

A hypothesis for the development of peritonitis in IPD is that inoculation of the peritoneal cavity can occur transluminally during manipulation of the dialysis system (*ie* bag changes, venting the system to air, addition of drugs to the dialysis bag), during catheter insertion, via seeding of the peritoneal cavity during bacteremia and via transcolonic and periluminal catheter spread of organism (Vas, 1985). The resulting organisms producing contamination are those related to the prevailing flora of the patient, medical personnel and that of medical equipment and atmospheric contamination. Those patients with inadequate host-defense mechanisms (such as patients with depressed immune systems from severe comorbid diseases) may be unable to clear the inoculum, especially during instances of seeding with large inocula or with very virulent organism and may thus develop peritonitis. The surveillance culture data suggest that host defence mechanisms play a significant role in the clearance of bacterial inoculation. From CAPD data, contamination of the peritoneal cavity is a common occurrence with a relatively low rate of true infection. It was found that there is a peak coincident between positive surveillance cultures and the high-risk period of peritonitis. In addition the distribution of organisms in the surveillance cultures is similar to that of peritonitis cases. This suggests that positive surveillance cultures, indeed, represent instances of true peritoneal contamination. The significantly higher incidence of frequent catheter manipulation and/or catheter leakages amongst IPD sessions with peritonitis ($p < 0.001$) as compared to IPD session without peritonitis may reflect the larger and continuing seeding of organism and probably nosocomial infection.

Stewart *et al* (1966) and Schwartz *et al* (1967) have recorded gram-negative organisms as the primary pathogen causing peritonitis in acute PD. Others have quoted gram-negative and gram-positive organisms with equal frequency (Vanmode *et al*, 1975; Delapenha *et al*, 1991). In our study, gram-negative infections were seen twice more

often than gram-positive infection. Some workers contend that transmural migration of bacteria through the intestinal wall is an important source of gram-negative infection during peritoneal dialysis (Schwartz *et al*, 1967; Vas, 1985). Although this cannot be denied, we feel that nosocomial infection of peritoneal fluid by skin contamination during manipulation of dialysis catheter (or leakages) is an equally important factor. Another observation is the relatively high incidence of peritonitis amongst our IPD sessions compared to other recent studies mentioned earlier. Our patient population may be different from those described in the western studies on peritonitis amongst IPD patients. Apart from the system of dialysis used being that of unprotected spikes and probably higher nosocomial infection in our hospital, the large proportion of chronic/end stage renal failure and diabetic patients (95% and 61.6% respectively) in our patient population may be contributory factors.

As a conclusion, we find that peritonitis is quite a frequent complication amongst our IPD patients but still comparable to other published reports. Further reduction in the frequency of peritonitis could be best achieved by scrupulous attention to aseptic technique by all workers caring for these patients, and by reducing the frequency of catheter manipulation. To prevent leakage, small puncture wounds should be made in the abdomen when dialysis was begun. The duration of peritoneal dialysis should be limited to 48 to 74 hours unless strong indications exist for continuation of dialysis for a longer period. The empirical use of cloxacillin in combination with an aminoglycoside or a cephalosporin appears appropriate and cost-effective until culture reports are available. These recommendations however should be reviewed in light of future changes in antibiotic susceptibilities.

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