Peritonitis: limiting the damage

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Reducing the morbidity associated with peritonitis is one of the major challenges to improve outcomes for patients on peritoneal dialysis (PD). In the short-term, during the actual episode, patients suffer pain, risk of hospitalization and social inconvenience, with extra and often numerous hospital visits. In one series, peritonitis accounted for 25% of hospital admissions for patients on PD [1]. In the long term, peritonitis is a major cause of patients transferring to haemodialysis, accounting for 13–54% of technique failure in long-term continuous ambulatory peritoneal dialysis (CAPD) patients [2] and 43% of patients on automated peritoneal dialysis (APD) [3]. Even in patients who recover from the initial episode, peritonitis causes other long-term sequelae, such as changes in membrane permeability and sclerosing peritonitis, which eventually contribute to technique failure.

Severe or repeated episodes of peritonitis are particularly damaging to the peritoneal membrane. Davies et al. [4] showed that in the short term, single episodes had no significant effect on membrane permeability or ultrafiltration, while recurrences or clusters of infection caused an increase in membrane permeability and reductions in ultrafiltration. Interestingly, these changes were more marked with higher cumulative dialysate leukocyte counts, independently of the infecting organisms. Longitudinal studies have not shown that these effects on membrane transport persist for the long term (over years) [4,5]. However, such studies are difficult to interpret. Patients with severe peritonitis will probably not be included either because of poor ultrafiltration, or because of another episode of peritonitis. There is one study, though, that does suggest a subtle long-term ultrafiltration dysfunction after a single episode of peritonitis [6]. *In vitro* evidence shows that there are pathways from acute inflammation to longer term fibrosis and angiogenesis in the peritoneum that would explain the association between peritonitis and ultrafiltration dysfunction [7].

Sclerosing peritonitis is a rare but devastating complication in patients on PD. Mortality is high, with rates of 37.5% being reported [8]. Although sclerosing peritonitis is a complication predominantly of long-term PD, with most cases occurring after 5 years [8], peritonitis is also an important predisposing factor. A recent large multicentre study from Japan showed that 30% of patients with early-onset sclerosing peritonitis (before 10 years) was associated with peritonitis, though this was not true with onset after 10 years on PD. The Australian data also suggest that around a third of cases are directly associated with an episode of peritonitis [9].

Minimizing the impact of peritonitis in the patient on PD will have a considerable effect on their experience of PD and will also extend their time span on this modality. Several strategies are required to achieve this as shown in Box 1.

**Reducing the incidence of peritonitis**

Peritonitis rates vary from centre to centre and are largely determined by patient selection, quality of patient training and social factors. Despite early reports when patients were carefully selected for APD, there is no consistent difference between peritonitis rates for CAPD and APD. There have been some advances. Regular use of mupirocin at the exit site...
of depression can reduce the rate of peritonitis. Associated with problems in patient technique. Further that Gram-positive infection is more commonly associated with a change in social circumstances, e.g. death or illness of a spouse, underdiagnosis, increasing frailty in the elderly and depression. A recent study of a large urban PD programme showed that depression and not age, diabetes or race was associated with a higher risk for peritonitis [12]. In the population studied, the peritonitis rate in non-depressed individuals was one in 23.4 patient-months compared with one in 11.5 patient-months in those who were depressed (45% study population). Interestingly, this was only true for Gram-positive and not for Gram-negative organisms; this may be partially explained by the fact that Gram-positive infection is more commonly associated with problems in patient technique. Further studies need to be done to determine whether treatment of depression can reduce the rate of peritonitis.

**Reducing morbidity and hospitalization**

The main symptom of peritonitis is abdominal pain. Often this is mild and resolves quickly after starting antibiotics. More severe pain needs to be recognized and treated with appropriate analgesia. Hospitalization is required if the patient is not responding to treatment or cannot administer their own antibiotics. Standard treatment for peritonitis is with intraperitoneal antibiotics. Many units still administer these with every exchange so patients who cannot do this are admitted to hospital. Furthermore, there are still those who change patients from APD to CAPD for peritonitis treatment; this usually means that the patient has to be hospitalized as they may not know how to perform CAPD and will not have the necessary supplies at home. Use of once-daily antibiotic administration for both CAPD and APD avoids these problems; patients can take home pre-injected bags and stay on their usual PD regime. Cure rates using such an approach [13,14] are identical to other published series using more conventional treatment regimes.

**Improving the cure rate**

The cure rate of peritonitis is only ~80% and is independent of the broad-spectrum antibiotic regime used. This cure rate would not be acceptable for many other forms of infection. There are several reasons for this: delay in starting antibiotics from the start of infection; presence of the catheter; and impaired functioning of peritoneal defence mechanisms. The need to seek medical help as soon as the patient notices cloudy fluid is part of training that PD patients need, and should be reinforced. However, there is evidence that when the fluid becomes cloudy, infection has already been present for 24h with positive bacterial cultures and increased peritoneal macrophages and neutrophils [15].

There is no data on whether different types of catheter are associated with different cure rates. Silver-impregnated catheters have been developed in an attempt to reduce infection rates, but no differences in peritonitis or exit site infection rates were observed in a randomized controlled trial [16].

There is more optimism regarding the possibility of improving peritoneal defence mechanisms. The phagocytic and killing capacity of peritoneal macrophages extracted from peritoneal effluent in patients using lactate dialysate is significantly improved when the pH of the dialysate is less acidic [17]. Lactate, itself also affects cellular function. In vitro studies have shown that the incubation of polymorphonuclear leukocytes in fluids containing 35mmol lactate at pH 5.2 resulted in an immediate and profound lowering of the intracellular pH which was not observed in lactate-containing fluids at neutral pH or at low pH in the absence of lactate [18]. The use of more biocompatible dialysate in patients has also been shown to improve peritoneal macrophage function. In vitro studies of peritoneal macrophages, which were extracted from peritoneal effluent at the end of a 6 month randomized study comparing bicarbonate/lactate and standard lactate dialysate, showed improved function in patients using the more biocompatible bicarbonate/lactate fluid [19].

Although the in vitro data on macrophage function are encouraging, there remain few data about the effect of using biocompatible fluid on actual peritonitis rates as there has been no large long-term randomized study. The phase 3 randomized study comparing bicarbonate/lactate and standard lactate dialysate enrolled only 106 patients and was for a 6 month period [20]. Peritonitis rates were not different during the study for the two groups. Around half the patients entered an extension study; this showed a significantly lower peritonitis rate (one out of 51 patient-months) for the bicarbonate/lactate group.
compared with one out of 19 patient-months for the control group. This is clearly very encouraging but needs to be confirmed, though personal experience also suggests a much lower peritonitis rate for patients using bicarbonate/lactate fluid.

Reducing the inflammatory response of the membrane

The use of more biocompatible dialysate may reduce the long-term inflammatory response of the peritoneal membrane to peritonitis, but as yet there are no studies looking at peritoneal transport related to peritonitis in patients using the new solutions.

Appropriate removal of the catheter with non-responding peritonitis

Failure to respond to treatment for peritonitis is associated with considerable morbidity and even mortality. Prolonged hospitalization often ensues because of complications such as ileus, intra-abdominal abscesses, wound infections, difficulties with establishing vascular access for haemodialysis and social/rehabilitation problems. We have shown that the factors associated with prolonged hospitalization were age and days of peritonitis before catheter removal [21]; the mean number of days with peritonitis in patients discharged within 10 days was 2.7 days compared with 7.5 days in patients in hospital for >10 days. Outcomes would therefore be considerably improved with early recognition of persistently cloudy fluid and prompt catheter removal.

Conclusion

There is much we can do now to limit the damage from peritonitis. The incidence of peritonitis will be reduced by the use of guidelines for patient and staff training and appropriate use of prophylactic antibiotics. Hospitalization and morbidity associated with peritonitis can be improved by using once-daily antibiotics. Early removal of the catheter in patients failing to respond to treatment will also reduce morbidity. Time will tell us whether clinical use of biocompatible dialysate will reduce not only peritonitis rates but also the changes to peritoneal membrane structure that follow on from infection.

Conflict of interest statement. None declared.

References