Peritoneal dialysis underscores its merits in portal hypertension-related and nephrogenic ascites

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ABSTRACT

In the Western world, peritoneal dialysis (PD) is less frequently applied as substitute therapy in end-stage renal disease (ESRD). In the Netherlands the use of PD has decreased from 30.3 to 13.5% due to several factors, but not due to lower PD-related outcome. The lower penetrance of PD diminishes experience with and exposure of young professionals to this treatment modality. This does not enhance a free and motivated choice among renal replacement therapies for patients who cannot be transplanted pre-emptively. To rejuvenate interest in PD and to underscore its merits, we would like to share the use of PD on two extraordinary occasions, where PD was the only option: one with portal hypertension-related ascites and profound gastrointestinal bleeding, and one with nephrogenic ascites. They pose difficult management problems that were favourably resolved by PD.

CASE 1

A 52-year-old Afro-American female presented in 2003 with nephrotic syndrome due to systemic lupus erythematosus nephritis class V complicated by portal vein thrombosis. Her renal disease responded well to treatment with glucocorticoids and azathioprine. A liver biopsy performed later that year revealed disturbed microcirculation due to portal vein thrombosis. An uneventful period followed. However, from 2013 onwards, she was frequently admitted because of profound haematemesis and tense ascites, which required multiple rubber band ligation sessions and percutaneous drainage, respectively. A transjugular intrahepatic portosystemic shunt was impossible because all major branches of the portal vein were occluded and surgical intervention was too risky in function, lower healthcare costs and improved quality of life and patient satisfaction. Despite this, the percentage of patients performing PD has declined in most Western countries. In the Netherlands PD use has decreased from 30.3 to 13.5% in the past 15 years. This has been ascribed to increased living related and unrelated organ donation and more investments in haemodialysis chairs, but not to a lower PD-related outcome. Training in and exposure to PD is a major concern with the decreasing numbers of PD patients, both for young nephrologists and for nurses. This hampers the free and motivated choice of patients requiring renal replacement therapy between the available options. To rejuvenate interest in PD and to underscore its merits, we present two extraordinary cases where PD was the only option: one with portal hypertension-related ascites and profound gastrointestinal bleeding, and one with nephrogenic ascites. They pose difficult management problems that were favourably resolved by PD.

KEYWORDS

Ascites, peritoneal dialysis, dialysis, nephrogenic ascites, portal hypertension, quality of life

INTRODUCTION

For patients requiring renal replacement therapy because of end-stage renal failure, dialysis and renal transplantation are the treatment options available. Peritoneal dialysis (PD) is complementary to haemodialysis with at least comparable survival, better preservation of residual renal function, lower healthcare costs and improved quality of life and patient satisfaction. Despite this, the percentage of patients performing PD has declined in most Western countries. In the Netherlands PD use has decreased from 30.3 to 13.5% in the past 15 years. This has been ascribed to increased living related and unrelated organ donation and more investments in haemodialysis chairs, but not to a lower PD-related outcome. Training in and exposure to PD is a major concern with the decreasing numbers of PD patients, both for young nephrologists and for nurses. This hampers the free and motivated choice of patients requiring renal replacement therapy between the available options. To rejuvenate interest in PD and to underscore its merits, we present two extraordinary cases where PD was the only option: one with portal hypertension-related ascites and profound gastrointestinal bleeding, and one with nephrogenic ascites. They pose difficult management problems that were favourably resolved by PD.

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view of her comorbidity. Ascites and oedema formation were treated with high doses of diuretics, large-volume paracenteses, and intravenous infusions of albumin. Her kidney function deteriorated intermittently and her quality of life steeply (Karnofsky score 20-30). On physical examination the patient showed normal blood pressure but tense ascites with collateral circulation reflected in abdominal wall veins. Apart from this, her physical examination was unremarkable.

Laboratory investigation showed normal liver function and enzymes, creatinine 5.7 mg/dl, and urea 70 mg/dl. Endogenous creatinine clearance was 12 ml/min with a proteinuria of 0.5 g/24 h. Serum albumin was 37 g/l, ascites albumin 9 g/l, and the serum ascites albumin gradient (SAAG) was 28 g/l. The ascites white blood count was 0.1 x 10⁹/l. Abdominal echography showed portal vein thrombosis with collateral vasculature, a hepatopetal flow and ascites. Endoscopy revealed bleeding varices that were treated by multiple banding sessions. Echocardiography revealed no cardiac failure or cardiac inflow obstruction. Because of refractory ascites, the need for frequent large volume paracenteses, deteriorating renal function, low quality of life and frequent hospitalisation PD was started. After drainage of ascites a Swan-neck Tenckhoff catheter was laparoscopically placed without complications. Initially, drainage of the ascites was started and gradually PD fluid was introduced to achieve a negative fluid balance. No episodes of hypotension or peritoneal fluid leakage were observed. A schedule with four exchanges a day of 1.5 litres of 1.36% glucose-containing peritoneal dialysis fluid was initiated. A peritoneal equilibration test performed after 4-6 months of dialysis disclosed a high ultrafiltration and a high solute transport pattern. The 24-hour dialysate protein content was 1 g/l.

In the following year she had no peritonitis or other PD-related complications. There were no episodes of oedema, and she presented less frequently with bleeding episodes. Endoscopic studies showed diminishing gastric and oesophageal varices. Liver function tests remained normal. At present, the patient maintains a residual diuresis of 1100 ml, a renal creatinine clearance of 7 ml/min, and an adequate Kt/V (measure of dialysis dose) of 2.2. Her serum albumin is stable at 37 g/l.

Hospitalisation rate decreased tremendously (from 55 days/year in the year prior to PD to 14 and 0 days/year in the two consecutive years with continuous ambulatory PD, respectively) and her clinical condition as well as her quality of life increased favourably (Karnofsky score improved from 20-30 to 70).

CASE 2

A 61-year-old Afro-American man with diabetes mellitus type 2 was treated with intermittent haemodialysis three times weekly because of end-stage diabetic nephropathy since 2002. In 2006 he presented with collapse and hypoxaemia. A pulmonary embolism was ruled out by CT scan, which showed pericardial and pleural effusion. In addition, ascites, hypalbuminaemia and hypotension were noted. His Kt/V was adequate (1.3 per dialysis), but daily haemodialysis and isolated ultrafiltration were necessary because of overhydration. Echocardiography revealed a good left and right ventricular function, no valve abnormalities, and pericardial effusion of 1 cm all around without inflow obstruction.

Ascites culture and cytology were negative, including a polymerase chain reaction for typical and atypical mycobacteria. The ascites was a straw-coloured exudate, had a white blood cell count of 0.1 x 10⁹/l and a SAAG of 1 g/l. Liver function tests, iron studies, thyroid-stimulating hormone, and parathyroid hormone were normal. No evidence was found of portal hypertension, cardiac or pericardial disease, peritoneal infection or malignancy. Nephrogenic ascites was diagnosed. Because of refractory ascites and inability to continue or intensify haemodialysis due to hypotension, a PD catheter was placed laparoscopically following intermittent drainage of ascites. A peritoneum biopsy was performed, which showed minor nonspecific chronic inflammation.

PD was started in the supine position with low intraperitoneal volumes that were gradually incremented. Protein loss in 24-hour dialysate decreased from 24 g/l to 1 g/l.

He became anabolic and normotensive (120/70 mmHg) with a desired dry weight gain of 5 kg. His Karnofsky score increased from 20 to 70. After two months a peritoneal equilibration test was performed, which showed a high average transport pattern that remained stable over the years. His Kt/V was 1.8. He continued on PD for eight years, his clinical course was not uneventful (amputation of both lower legs in 2008, peritonitis due to S. aureus in 2013). He died due to myocardial infarction following peritonitis in 2014.

DISCUSSION

PD was successful in both cases for a number of reasons: the patients felt much better because the mechanical problem of ascites was no longer present, caloric and protein intake increased with a subsequent rise in lean body mass. In addition it ensured continuous control of salt, water balance and uraemia. There are a few things to keep in mind when considering PD in patients with ascites. First, if there is significant abdominal wall oedema, it may result in delayed wound healing. It is prudent to have a longer break-in period. Secondly, not all the ascites fluid should be drained at once. Thirdly, distended abdominal wall veins must be taken into
account when choosing the placement site of ports and of the PD catheter.

In our first patient the ascites was due to portal hypertension subsequent to portal vein thrombosis with a SAAG of 28 g/l. Patients with portal hypertension requiring dialysis for acute or chronic renal failure pose management challenges.\textsuperscript{6,7} PD offers several advantages over haemodialysis (no anticoagulation, normalised bleeding time). Excessive bleeding following catheter placement and excessive protein loss have been mentioned as possible drawbacks, but this has not been well documented in the literature. The protein content of ascitic fluid in patients with portal hypertension is generally low and the contribution of protein losses with dialysis fluid to malnutrition in such patients is uncertain at best. The high ultrafiltration and solute removal rate corresponds to a high peritoneal permeability, which can be attributed to an increase in the peritoneal surface area related to portal hypertension.\textsuperscript{8} Our patient did not show hepatic failure and was successfully controlled with a progressively negative fluid balance during PD. Insertion of foreign bodies in the abdominal cavity including peritoneovenous shunts has been abandoned by the hepatology community due to the high risk of catheter occlusion and infection. Fortunately our patient did not sustain any peritonitis and protein losses decreased (from 9 g/l in ascites to 1 g/l in dialysate) during follow-up, maintaining serum albumin levels. At present she feels well. PD appears cost-effective with respect to hospitalisation rate, morbidity and quality of life.

Our second patient suffered from nephrogenic ascites. This is a rare and poorly understood condition characterised by refractory ascites in a patient with end-stage renal disease, where portal hypertensive, infectious and malignant processes have been excluded.\textsuperscript{9-11} Pathophysiological factors associated with nephrogenic ascites include chronic fluid overload, changes in peritoneal permeability and impaired lymphatic peritoneal resorption in uraemia.\textsuperscript{7,12} Contributing factors may be hypoproteinaemia, hyperparathyroidism, congestive heart failure, constrictive pericarditis, pancreatitis or cirrhosis with portal hypertension.\textsuperscript{11}

Diagnosis is made by exclusion of other causes. The ascitic fluid (high protein content, low SAAG, and low leukocyte count) is typically an exudate.\textsuperscript{7} This narrows the aetiological possibilities to tuberculous peritonitis, pancreatitis, malignancy, and nephrogenic ascites. Histological examination of the peritoneum often reveals chronic inflammation and mesothelial cell proliferation with variable degrees of fibrosis.\textsuperscript{8,9,12-14} A peritoneal biopsy in our patient showed chronic nonspecific inflammation. In the treatment of nephrogenic ascites salt and water restriction, vigorous haemodialysis with isolated ultrafiltration and intravenous albumin infusion has been advocated,\textsuperscript{14} but this is not always effective\textsuperscript{11} and severe hypotension may become the limiting factor,\textsuperscript{9} as was the case in our patient. A peritoneovenous shunt has been shown to improve nephrogenic ascites,\textsuperscript{9,15} but is not free of complications.\textsuperscript{8,16} PD relieved the ascites and favourably improved the condition of our second patient. The reduction of protein loss in both patients, but especially in the second case, remains unexplained but is of clear benefit. PD has been shown to resolve ascites by reducing the intraperitoneal fluid protein concentration which draws fluid into the peritoneal cavity by oncotic forces.\textsuperscript{12}

Renal transplantation is the most effective treatment for nephrogenic ascites: almost all reported cases had complete resolution of the ascites within 2-6 weeks.\textsuperscript{7,8} This observation argues for a disturbed fluid balance as the primary cause. Our patient was not willing to accept a kidney transplant, and at presentation there were medical contraindications to transplantation.

The appearance of nephrogenic ascites was believed to indicate an extremely poor prognosis.\textsuperscript{9,8,16} One year after the development of nephrogenic ascites a third of patients have died.\textsuperscript{11} Today, however, the prognosis is certainly much better. Though renal transplantation appears the cure, PD is a readily available, effective treatment that relieves ascites and improves both the clinical condition of patients with nephrogenic ascites and their quality of life.

In conclusion, two challenging refractory ascites cases are presented: one with hepatorenal disease and one with nephrogenic ascites. They posed difficult management problems that for a prolonged period were favourably resolved by PD. Also for less extraordinary cases, initiating renal replacement therapy on PD was associated with favourable survival outcomes when compared with starting on haemodialysis treatment.\textsuperscript{9,16} In the absence of medical or social contraindications, PD can offer other important benefits, including patients' autonomy and lower costs.\textsuperscript{6} Furthermore, for the growing group of elderly patients, PD has a number of advantages and most of the perceived barriers to PD may be overcome.\textsuperscript{7} In addition, for the rising numbers of those suffering from end-stage heart failure refractory to available therapies, PD may be an effective, cost-effective and safe therapeutic option for fluid control, improving heart function while preserving residual renal function with less hospitalisations and better quality of life.\textsuperscript{9} To be readily available, a certain penetration of and expertise in PD as renal replacement therapy is warranted. Increasing collaboration between different centres to keep a high level of knowledge in PD and to explore the reasons for not selecting PD as initial dialysis modality will be needed. In this way the adagium of a free and motivated patient choice among all renal replacement modalities can better be met.
DISCLOSURES

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Informed consent was obtained from the patients for publication.

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