NUTRITION CHANGES IN CONSERVATIVELY TREATED PATIENTS WITH ENCAPSULATING PERITONEAL SCLEROSIS

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◆ **Background:** Encapsulating peritoneal sclerosis (EPS), a rare but serious complication of long-term PD, is characterized by nausea, abdominal pain, weight loss, anorexia, and constipation. It can cause a significant deterioration in a patient's nutrition status. In the present study we examined changes in nutrition status and outcomes for patients with EPS treated conservatively without the use of surgical intervention.

◆ **Methods:** Patients diagnosed with EPS at our institution between December 2006 and December 2010 were identified, and data on demographics, nutrition, and symptoms were collected every 2 months for 12 months and then at 18 and 24 months.

◆ **Results:** Of the 15 patients identified, 12 were malnourished or at risk of malnutrition according to their subjective global assessment score, with 11 of the 15 presenting with more than 10% weight loss in the 6 months before diagnosis. Furthermore, symptom burden was high, with 11 of 15 patients reporting 2 or more gastrointestinal symptoms.

Of the 15 patients, 12 required parenteral nutrition for a median of 4.5 months, and 5 died within the first 12 months after diagnosis. In the 10 survivors, albumin and C-reactive protein significantly improved over the 24 months after diagnosis. Improving trends in weight and symptoms were also observed in those patients.

◆ **Conclusions:** In some patients with EPS, a conservative approach without surgical intervention, and with regular dietetic input and aggressive nutrition support, can lead to improved nutrition status and symptoms.

Encapsulating peritoneal sclerosis (EPS), a serious but uncommon complication of long-term peritoneal dialysis (PD), is characterized by bowel obstruction and encapsulation because of the formation of a fibrous cocoon arising from the peritoneal membrane. Clinical features include nausea, vomiting, abdominal pain, reduced appetite, constipation, and ascites. Not surprisingly, nutrition status is often compromised in these patients. The development of EPS is associated with high mortality. In the largest UK cohort of patients with EPS, 53% died over a 10-year period (1). Mortality in other countries varies: A multicenter study conducted in Japan reported deaths in 38% of patients over a 4-year period (2). In Korea, 24% of patients died over a 20-year period (3).

Although a variety of treatments have been used in EPS, evidence to support them is lacking, and there is no uniformly accepted treatment option. The use of drugs such as corticosteroids, other immunosuppression agents, and tamoxifen is based mostly on anecdotal reports. The largest case series of patients with EPS is a retrospective study from the pan-Thames audit group, which showed no difference in outcomes for patients treated with any of the foregoing drugs singly or in combination compared with patients receiving no drug treatment (1).

Surgery has also been used to treat EPS, and evidence that this intervention can have a beneficial outcome and potentially be curative is increasing (4). Surgery, however, is invasive and difficult to perform, and is associated with serious morbidity and mortality risks. Furthermore, encapsulation may recur, requiring repeat surgery. Surgery should therefore be performed only in specialist centers.

Given the limited evidence of benefit with drug treatment and the risks associated with surgery, conservative management with nutrition support may often be the only option. In the pan-Thames series, very few patients had undergone surgery. About a third received

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parenteral nutrition (PN), and that group had the worst outcomes—which is not surprising, because it would also have consisted of the sickest patients (1). At our center, the policy of the renal physicians has been not to refer patients with EPS for surgery because local expertise is lacking, and there is a paucity of published UK data on outcomes after surgery. Those circumstance therefore provide an opportunity to prospectively determine patient outcomes, focusing on nutrition status, in a group of patients managed solely with active nutrition support.

METHODS

For the period December 2006 to December 2010, all patients diagnosed with EPS at Imperial College Renal and Transplant Centre were identified. The diagnosis was suggested by clinical symptoms consistent with bowel obstruction and confirmed by positive computed tomography imaging using the criteria published by Tarzi *et al.* (5). Data were collected at baseline, every 2 months for the first year, and then at 18 and 24 months.

DEMOGRAPHIC AND CLINICAL DATA

Baseline demographic data collected included age, sex, renal replacement treatment at the time of diagnosis, length of time on PD, time from stopping PD to diagnosis, and time from diagnosis to the start of the study. At each time point, patients were asked whether they had been experiencing the following 5 gastrointestinal (GI) symptoms: nausea, vomiting, abdominal pain or cramps, constipation, and diarrhea.

NUTRITION ASSESSMENT

The nutrition data collected at each time point included height, weight, body mass index, handgrip strength, plasma albumin, and the 7-point subjective global assessment (SGA) score. Actual weight was used for transplant patients and dry weight for hemodialysis (HD) patients. In the few patients in whom ascites was present, an estimation of water weight was made and subtracted from the actual or dry weight (6). Height was measured for all patients using a stadiometer. Body mass index was calculated as weight in kilograms divided by the square of height in meters. Handgrip strength was measured on the nondominant arm (or dominant arm, in patients with a fistula) using a single-spring handgrip dynamometer (Grip-D: CMS Weighing Equipment, London, UK). Patients held the dynamometer at thigh level and the maximum grip strength of three readings was taken. Plasma albumin was measured using the bromocresol purple albumin

assay. The 7-point SGA score was used to estimate nutrition status because the SGA has been validated in dialysis patients (7). This composite score is based on a variety of factors, including weight and weight change, dietary intake, GI symptoms, functional capacity, disease state, and a physical examination.

STATISTICAL ANALYSIS

For continuous data, paired or unpaired t-tests were used to compare the mean differences between groups. For non-continuous data, the Fisher exact test was used.

RESULTS

DEMOGRAPHICS

During the study period, 15 patients (9 men, 6 women) developed EPS. In 8 patients, the diagnosis was made after transfer to HD; in 6, after kidney transplantation; and in 1, while that patient was still on PD. Mean age of the patients was 59.2 ± 15.16 years, and mean duration of PD was 6.3 ± 1.28 years. Mean time from stopping PD to diagnosis (where applicable) was 3.0 ± 3.10 months.

CLINICAL PARAMETERS

The causes of renal failure in the 15 patients were unknown ($n = 6$), glomerulonephritis ($n = 3$), hypertension ($n = 2$), diabetic nephropathy ($n = 1$), immunoglobulin A nephropathy ($n = 1$), Alport syndrome ($n = 1$), and reflux nephropathy ($n = 1$). A history of diabetes was present in 3 patients, and a history of cardiovascular disease, in 5.

Drug treatment was used in 9 patients, with all 9 (6 of whom were transplant patients) receiving immunosuppression agents; 2 of the patients also received tamoxifen. As mentioned earlier, no patients were referred for surgery. A high symptom burden was reported at baseline, with 11 of the 15 patients reporting the presence of 2 or more GI symptoms. Patients reported abdominal pain and bloating ($n = 10$), vomiting ($n = 8$), nausea ($n = 7$), constipation ($n = 7$), and diarrhea ($n = 3$).

NUTRITION ASSESSMENT

Table 1 shows the baseline data on nutrition status for the 15 patients. Most of the patients were considered malnourished or at risk of malnutrition (SGA score of 5 or less). Furthermore, significant weight loss was reported in 11 patients, who experienced the loss of more than

TABLE 1
Baseline Nutrition Status of Patients with
Encapsulating Peritoneal Sclerosis

Variable	Value ^a
Patients (<i>n</i>)	15
Malnourished/risk of malnutrition	12
≥2 Gastrointestinal symptoms	11
Weight (kg)	60.6±9.40
Body mass index (kg/m ²)	22.5±2.53
Weight change in preceding 6 months (%)	-12.9±11.35
Handgrip strength (kg)	16.4±8.05
Albumin (g/dL)	25.5±5.77
C-Reactive protein (mg/L)	84.9±59.3

^a Mean and standard deviation, except for patient numbers.

10% of body weight in the 6 months before diagnosis. Only 2 patients had normal levels of plasma albumin and C-reactive protein (CRP).

NUTRITION MANAGEMENT

At baseline, 14 of the 15 patients required nutrition support, with 6 requiring PN and 8 requiring oral supplementation. Of the latter 8 patients, 6 also required PN within the first 12 months. Thus, 80% of the patients (*n* = 12) required PN during the study. The median time on PN in these patients was 4.5 months (range: 0.4 – 22.7 months). In 5 of the patients, PN was given at home, for a total duration ranging from 9.3 to 22.7 months. Nasogastric feeding was initiated in 1 patient for 2 months until sufficient oral intake was maintained, at which point nasogastric feeding was discontinued. Nasojejunal feeding was used in 1 patient for 5 months, but because of severe GI symptoms, this approach had to be stopped and PN re-started.

Among the 12 patients requiring PN, 5 deaths occurred. Of the 12 patients, 3 had PN discontinued because of receiving palliative care only. At 24 months, 3 patients remained on PN; another 4 were able to discontinue PN after spontaneous resolution of bowel obstruction. Intradialytic PN was used in 1 patient for a short period and was stopped once the patient's nutrition status had improved.

Figure 1 illustrates changes in the methods of nutrition support in each of the 15 patients.

NUTRITION AND SYMPTOM CHANGES IN SURVIVORS

Mortality during the 2-year period was 33% (5 patients), with a median time from diagnosis to death

Figure 1 — Changes in the method of nutrition support over time. PN = parenteral nutrition; NG/NJ = nasogastric or nasojejunal feeding; ONS = oral nutrition support; None = no nutrition support.

of 4.6 months (range: 2.9 – 15.1 months). In 4 cases, death occurred within the first 6 months from diagnosis; 1 patient died at 15 months from diagnosis.

Table 2 presents the changes in nutrition from baseline to 24 months in the 10 survivors. Over the 24 months, plasma albumin significantly improved (+7.4 g/dL, *p* = 0.001) and CRP fell (-48.6 mg/L, *p* = 0.025). An improvement in weight was also observed. After the loss of approximately 12% of body weight at diagnosis, patients experienced a 3.4% gain in weight over 2 years. Those observations are consistent with a pattern of ill health at diagnosis, followed by a period of recovery post-diagnosis if the patient survives. Most patients who survived EPS were no longer at nutritional risk after 2 years.

In this patient group, GI symptoms were common. In the surviving patients, symptoms improved over the 2 years of the study, with just 2 patients experiencing 2 or more symptoms at the end of the study period, compared with 7 at baseline. There appeared to be little difference in the symptom burden at baseline between patients with a favorable outcome and those with a poor outcome, with 71% and 88% of patients respectively experiencing 2 or more symptoms.

BASELINE PREDICTORS OF OUTCOME

Patients were divided into two groups according to outcome. Group 1 included the patients with a favorable outcome (did not require PN or were able to stop PN and survive), and group 2 included the patients with a poor outcome (died or remained on PN at 24 months). Table 3 sets out the baseline demographic and nutrition parameters for each group. Although there were no significant differences between the two groups, group 2 tended to have a higher percentage weight loss at baseline, lower plasma albumin, higher CRP, a greater number of hospital days, and a much earlier need for PN. Patients

TABLE 2
Changes in Nutrition Status in Surviving Patients with Encapsulating Peritoneal Sclerosis

Variable	Baseline	Value ^a 24 Months	<i>p</i> Value
Patients (<i>n</i>)	10	10	
Malnourished/risk of malnutrition	7	2	0.67 ^b
≥2 Gastrointestinal symptoms	7	2	0.467 ^b
Weight (kg)	58.5±9.70	60.5±11.0	0.524 ^c
Body mass index (kg/m ²)	22.3±2.76	23.1±3.70	0.478 ^c
Weight change in preceding 6 months (%)	-11.8±13.63	3.7±3.84	0.004 ^c
Handgrip strength (kg)	18.0±8.02	20.6±8.09	0.196 ^c
Albumin (g/dL)	26.3±6.09	33.7±5.10	0.001^c
C-Reactive protein (mg/L)	76.4±57.55	27.8±45.45	0.025^c

^a Mean and standard deviation, except for patient numbers.

^b By Fisher exact test.

^c By paired t-test.

TABLE 3
Baseline Demographic and Nutrition Data by Outcome at 24 Months

Variable	Group 1 ^b	Value ^a Group 2 ^c	<i>p</i> Value
Patients (<i>n</i>)	7	8	
Malnourished/risk of malnutrition	5	7	0.446 ²
≥2 Gastrointestinal symptoms	4	7	0.231 ²
With diabetes	1	2	0.554 ^d
With cardiovascular disease	1	4	0.182 ^d
With early PN requirement (>3 months)	2	5	0.214 ^d
Age (years)	54.6 (19.40)	63.3 (9.86)	0.284 ^e
Time on peritoneal dialysis (years)	6.7 (0.98)	6.0 (1.49)	0.222 ^e
Dialysis modality at diagnosis (<i>n</i>)			
Hemodialysis	5	3	NA
Transplantation	2	4	
Peritoneal dialysis	0	1	
Weight (kg)	59.4±10.20	61.7±9.20	0.648 ^e
Body mass index (kg/m ²)	22.5±2.87	22.5±2.39	0.987 ^e
Weight change in preceding 6 months (%)	-10.8±15.65	-14.8±6.26	0.516 ^e
Handgrip strength (kg)	16.3±3.62	16.5±10.87	0.966 ^e
Albumin (g/dL)	28±6.61	23.4±4.21	0.125 ^e
C-Reactive protein (mg/L)	55.7±52.78	110.4±55.25	0.073 ^e
Pharmacologic treatment (<i>n</i>)			
Immunosuppression	3	6	NA
Tamoxifen	2	0	
Hospitalization (days)	82.9±92.57	163.63±123.22	0.180 ^e

PN = parenteral nutrition.

^a Mean and standard deviation, except for patient numbers.

^b Favorable outcome (no PN or able to come off PN).

^c Poor outcome (died or remained on PN).

^d By Fisher exact test.

^e By paired t-test.

with a kidney graft tended to fall into group 2, and those switching to HD, into group 1, although the numbers were too small for any statistical testing.

MANAGEMENT OF HOME PN PATIENTS

Long-term PN (9.3 – 22.7 months) was required in 5 patients, and so they were discharged home on PN. The major complication was line infection requiring a line change; the mean number of lines required by each patient was 4.2 (range: 3 – 6), representing a mean of 116.3 days (range: 2 – 307 days) per line. The 5 long-term PN patients had the greatest number of hospital days over the 24-month period, averaging 263 days, which included admissions for PN initiation and training, complications associated with PN (for example, liver dysfunction and line infections), and exacerbation of EPS symptoms.

DISCUSSION

Many published studies have looked at various aspects of EPS, including incidence, risk factors, treatment options, and outcomes. However, relatively few have reported data on the nutrition status and management of patients with EPS. In fact, only two retrospective studies have addressed the issue. In Korea, Kim *et al.* (8) classified nutrition status according to plasma albumin in 34 cases of surgically and conservatively managed EPS patients, and in the United Kingdom, data on weight, body mass index, and albumin were reported for surgically treated patients (9). The present study is therefore the only prospective examination and report on the nutrition status and management of patients diagnosed with EPS.

A thorough nutrition assessment is essential in patients with EPS. The UK Renal Association guidelines (10) suggest that weight alone is insufficient for that purpose, because of the frequent occurrence of abnormal fluid balance or ascites, or both. There are, however, no current recommendations about the optimal indices of nutrition to use. In addition to weight, we used a variety of anthropometric, biochemical, and functional markers, and also a composite score based on a clinical and physical examination. Plasma albumin is an important marker of nutrition in patients with renal disease, even in the presence of inflammation (11). At diagnosis, only 20% of our patients had normal plasma albumin—a result comparable to that reported in Korea (8). In the 10 surviving patients in our series, plasma albumin improved significantly (by 50% over 24 months); indeed, median plasma albumin at 2 years was within the normal range. Over a period of 6 months, improvements in plasma

albumin have also been reported in patients undergoing surgery for EPS, although that result was not statistically significant (9).

Other markers of nutrition also improved. A significant rise in weight was observed, with patients starting to gain weight by 12 months. Inflammatory status also improved, with a reduction in plasma CRP over the 2-year period. The data also suggest an improvement in SGA score. At diagnosis, 70% of patients were malnourished or at risk of malnutrition; after 2 years, only 20% were malnourished or at risk. However, the difference was not significant, probably because of the small sample size.

The UK Renal Association recommendations (10) consider early dietetic referral, with nutrition support by the oral, enteral, or parenteral route, to be essential for EPS patients. All our patients were referred at diagnosis, and 93% were started on nutrition support during the 2-year period after diagnosis. That support included oral supplements, nasogastric feeding, nasojejunal feeding, and PN. Parenteral nutrition is usually required in patients with severe EPS because of functional bowel obstruction; it was required in 80% of our patients. That proportion is much higher than the 35% of patients who received PN in the UK Pan-Thames EPS study (1), but comparable to the 78% of patients treated with PN in a large multicentric trial in Japan (12). Our higher rates of PN than those in the Pan-Thames study might be explained by the purposive initiation of more aggressive nutrition support than has historically been used in our center. Of the patients referred, 50% started PN at baseline, and a further 42% started within the first 6 months after diagnosis. Only 8% started PN between 6 and 12 months after diagnosis.

About half our patients were on concomitant drug treatment, chiefly immunosuppression for transplantation. Given the small number of patients overall, it is not possible to draw definitive conclusions about the potential effect of drug treatment on outcomes, but notably, patients on immunosuppression were included in both outcome groups. Our data show that conservative management, with nutrition support—most notably PN—and possibly pharmaceutical treatment, can achieve good outcomes, with an overall mortality rate of 22% at 1 year and 33% at 2 years. In comparison, the only UK study of EPS patients undergoing surgical intervention reported mortality of 30% in 23 patients (9).

In our study, patients presenting with higher CRP, lower albumin, and a higher percentage weight loss were more likely to have a poorer outcome. Such patients should be identified as early as possible, because they may benefit from early surgical intervention. It is also important to consider the impact of long-term PN on

quality of life. These patients first require a long initial hospital admission to stabilize on PN and to set up a home PN service. They may then require subsequent hospital admissions for their EPS and their PN complications, including line infection, liver dysfunction, and severe GI symptoms. In fact, our 5 home PN patients had a mean 8.2 hospital admissions and 263 hospital days over the 2-year period. In addition, many were either "nil by mouth" or able to tolerate only very small amounts of an oral diet. Although quality of life was not formally assessed in the present study, it is likely that both the foregoing factors could negatively affect a patient's quality of life. It is therefore essential that counseling be made available to all patients treated with home PN.

CONCLUSIONS

Many patients with EPS are able to maintain or improve their nutrition status and reduce GI symptoms with regular dietetic input and aggressive nutrition support. It is possible that early selection of patients for surgery when they are failing to respond to nutrition support alone or when they continue to depend on PN may result in an even lower mortality rate and improvement in quality of life.

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