Incidence and Outcomes of Home Parenteral Nutrition in Patients With Crohn Disease in Olmsted County, Minnesota

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Background: We sought to estimate the incidence of home parenteral nutrition (HPN) use in a population-based cohort of patients with Crohn disease (CD), and to assess clinical outcomes and complications associated with HPN.

Methods: We used the Rochester Epidemiology Project (REP) to identify residents of Olmsted County, who were diagnosed with CD between 1970 and 2011, and required HPN.

Results: Fourteen out of 429 patients (3.3%) with CD received HPN (86% female). Eleven patients (79%) had moderate–severe CD and 12 patients (86%) had fistulizing disease. Thirteen patients (93%) underwent surgery, primarily due to obstruction. Among CD incidence cases, the cumulative incidence of HPN from the date of CD diagnosis was 0% at 1 year, 0.5% at 5 years, 0.8% at 10 years, and 2.4% at 20 years. Indications for HPN included short bowel syndrome in 64%, malnutrition in 29%, and bowel rest in 21%. The median duration of HPN was 2.5 years. There was an average weight gain of 1.2 kg at 6 months, an average weight loss of 1.4 kg at 1 year, and a further weight loss of 2.2 kg at 2 years from the start of HPN. Patients were hospitalized a mean of 5 times after the start of HPN, mainly due to catheter-related bloodstream infections and thrombosis.

Conclusions: Less than 4% of patients with CD need HPN. Most have moderate to severe disease with short bowel syndrome or malnutrition. Possible reasons for the patients' weight loss could be noncompliance, and increased metabolic needs because of active disease.

Lay Summary

A small proportion of patients with Crohn disease need home parenteral nutrition (HPN). When deciding to initiate HPN, providers need to weigh the benefits and risks of HPN, and those who fail conventional therapy with ongoing malnutrition should be considered.

Key Words: inflammatory bowel disease, Crohn disease, home parenteral nutrition, epidemiology, nutrition

INTRODUCTION

Crohn disease (CD) is a type of inflammatory bowel disease (IBD) that can affect the gastrointestinal tract anywhere from the mouth to the anus. It affects the small intestine in 30%–40% patients, both small and large intestine in 40%–55% patients and the colon in 15%–25% patients.[1] Most patients with moderate to severe CD undergo at least 1 bowel resection (either small bowel or colon or both) during their clinical

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course. As the number and/or the extent of surgical resections rise, the possibility that the patient may become nutritionally compromised increases. Causes of malnutrition in patients with CD include poor intake of food (due to abdominal pain or anorexia), intestinal malabsorption, and drugs such as corticosteroids, immunosuppressants, and sulfasalazine.[2,3] Malnutrition has a further negative impact on such patients by causing cellular immunodeficiency, which could cause impairment of mucosal barrier and an increased risk of infection.[4,5] Therefore, giving parenteral nutrition might help to improve nutritional status and prevent malnutrition and reduce risk of infection.[6–8] Even though parenteral nutrition and home parenteral nutrition (HPN) have a limited role in the nutritional management of patients with CD, they are preferred treatments rather than enteral nutrition (EN) in patients with an obstructed bowel in which the feeding tube cannot be placed beyond the point of obstruction, short bowel syndrome (SBS), severe dysmotility, or cumulative inflammation.[9–13]

The primary aim of our study was to estimate the cumulative incidence of patients on HPN in a population-based inception cohort of patients with CD. We also sought to assess clinical outcomes of CD patients on HPN and the complications associated with this nutritional intervention.

METHODS

Study Design

This was a retrospective cohort study of Olmsted County, Minnesota residents diagnosed with CD between 1970 and 2011. The study protocol was approved by the Mayo Clinic and Olmsted Medical Center Institutional Review Boards. As per Minnesota state law, no medical record information was abstracted from the records of patients who had withdrawn authorization to review their medical records for research purposes. The resources of the Rochester Epidemiology Project (REP) were used to gather patient information. The REP is a unique medical health records linkage system generating diagnoses from outpatient visits, emergency room visits, hospitalizations, nursing home visits, surgical procedures, autopsy examinations, and death certificates. It exploits the fact that virtually all of the healthcare of residents of the county is provided by 2 organizations: Mayo Medical Center and Olmsted Medical Center. Previous studies have shown that in any given 4-year period, over 95% of the county population is seen at one of the 2 healthcare systems in the county.[14–16]

Study Population

In previous studies, we have used consistent definitions to identify all Olmsted County residents who were diagnosed with CD between 1940 and 2011.[17–19] This list of incidence cases of CD was cross-matched with a list of patients who had received HPN. For a description of clinical outcomes, we also identified prevalence cases of CD (ie, patients who had already been diagnosed with CD before moving into Olmsted County) who were also on HPN.

Data Collection and Data Analysis

Crohn severity was defined by a combination of endoscopic findings and symptoms. The medical records of potential cases were abstracted for the duration of HPN/total parenteral nutrition use, and the number of infusions per week. We also assessed the reason for parenteral feeding and the associated complications of HPN. A descriptive statistical analysis was performed. We also analyzed the change in weight, and concentrations of albumin, 1,25-dihydroxy Vitamin D, iron, folate, Vitamin B12, zinc, erythrocyte sedimentation rate, and C-reactive protein (CRP) before and at 6, 12, and 24 months after the start of HPN by Student *t* test. Among the incidence cases, we reported the estimated cumulative incidence of need for HPN from time of CD diagnosis using the Kaplan–Meier method.

RESULTS

In our study, 429 Olmsted County residents were diagnosed with CD between 1970 and 2011. Fourteen CD patients from Olmsted County received HPN between 1992 and 2018 (7 incidence cases and 7 prevalence cases). The patients were followed for a median of 16.9 years after diagnosis of CD [interquartile range (IQR), 12.3–24.7] and required HPN a median of 6.7 years after their diagnosis (IQR, 2.3–15.8).

Among the 14 patients receiving HPN, 12 were females (85.7%). Eleven patients (78.6%) had moderate to severe CD. The ileum was affected in 13 patients (92.9%), colon in 10 patients (71.4%), and there was proximal gastrointestinal involvement in 2 patients (14.3%). Twelve patients had fistulizing disease (85.7%). Thirteen patients underwent surgery at least once in Olmsted County. The indications for surgery are described in Table 1. The median number of bowel resections was 4 (range, 0–7). Twelve patients (81%) had stomas placed. Two patients were current smokers and 5 patients were former smokers.

TABLE 1. Indications for Surgery in Patients With CD Who Required HPN in Olmsted County, Minnesota

Indications for Surgery	Patient Number (Percentage)
Obstruction	11 (84.6%)
Fistulizing disease	6 (46.2%)
Severe pain	4 (30.8%)
Failure of medical therapy	6 (46.2%)
Bleeding	2 (15.4%)
Necrosis	2 (15.4%)
Abdominal abscess	3 (23.1%)

Among incidence cases, the cumulative incidence of HPN use from the date of CD diagnosis was 0.0% at 1 year [95% confidence interval (CI): 0.0%–1.8%], 0.5% at 5 years (95% CI: 0.1%–2.0%), 0.8% at 10 years (95% CI: 0.3%–2.5%), and 2.4% at 20 years (95% CI: 1.1%–5.1%) (Fig. 1). The median duration of HPN use was 2.4 years (range, 40 days to 16.4 years). Four patients were still on HPN at the time of last follow-up. Among the 4 still on HPN at last follow-up, the median duration of HPN was 7.4 years.

Eight patients had a single lumen Hickman line (57.1%), 4 patients had an intravascular access device (28.6%), 1 patient had a single lumen peripherally inserted central catheter (PICC) line placed (7.1%), and 1 patients had a double lumen PICC (7.1%). Indications for HPN included SBS in 9 patients (64.3%), malnutrition in 5 (3, 5.7%), and bowel rest in 3 patients (21.4%) (Table 2). The median length of small bowel remaining was 105 cm (IQR, 87.5–157.5).

The mean number of hospitalizations after the start of HPN was 6 (range, 0–20). Ten patients (71.4%) had catheter-related blood stream infections (CRBSIs) and 3 (21.4%) patients (18%) had line-related thrombosis. Five patients had osteoporosis and 2 had osteopenia. Parenteral nutrition-associated liver disease occurred in 3 patients (21%). By 6 months after starting HPN, 3 patients had experienced CRBSI and 3 had experienced thrombosis. By 12 months out from start of HPN, an additional 3 patients had experienced CRBSI, 3 were noted to have osteoporosis, and 1 was noted to have liver injury. By 2 years out, there were 4 additional CRBSI, 2 more patients with osteoporosis, and 2 more patients with liver injury. Only one patient required insulin while on HPN. The patients received a mean nutrition of 22.3 kcal/kg/d (95% CI: 18.2–26.4). There was an average weight gain of 1.1 kg (95% CI: −1.9 to 4.2) at 6 months, an average weight loss of 1.4 kg (95% CI: −5.4 to 2.6) at 1 year, and a further weight loss of 1.7 kg (95% CI: −5.5 to 2.1) at 2 years from the start of HPN. Patients started to lose weight after 6 months of HPN initiation. The decrease from baseline remained significant at 1 year (*P*-value: 0.005). Weight changes were not significantly different from baseline beyond 1 year after HPN. Steroid tapering (29%), infection (mostly CRBSI) (64%), and bowel resection (21%), were the main possible reasons for weight loss. Five patients died mainly due to CD.

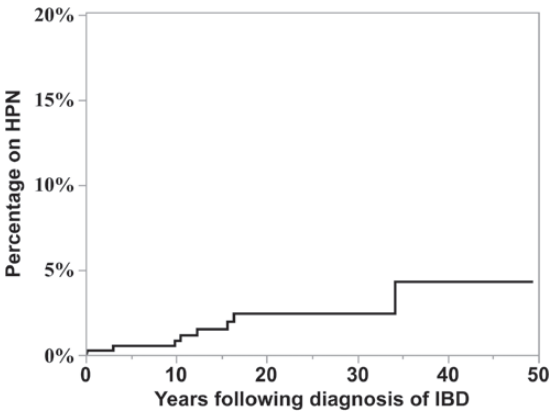

FIGURE 1. Cumulative incidence of need for HPN among 429 Olmsted County residents with CD, from the date of Crohn diagnosis. P.s: patients who had missing last follow-up were excluded.

At the time of starting HPN, the patients' mean albumin was 3.3 g/dL (95% CI: 3–3.5). During HPN, albumin significantly increased, such that the mean levels at 6, 12, and 24 months were 3.8 g/dL (95% CI: 3.4–4.1, *P*-value: 0.01), 3.9 g/dL (95% CI: 3.5 .3, *P*-value: 0.002), and 4 g/dL (95% CI: 3.7–4.4, *P*-value: 0.002), respectively. The median concentrations of 1,25-dihydroxy Vitamin D, iron, folate, Vitamin B12, zinc, erythrocyte sedimentation rate, and CRP, and their 95% CI at 6, 12, and 24 months after HPN are listed in Table 3. In most cases, the laboratory parameters improved over time, and the mean CRP decreased.

DISCUSSION

In this community-based inception cohort, we found that the cumulative incidence of need for HPN in CD patients was small—0.5% at 5 years after the diagnosis of CD, increasing to 2.4% at 20 years after diagnosis. Most patients were females with moderate to severe disease affecting the ileum, and fistulizing behavior was common. The main indications for HPN were SBS and malnutrition. More than 85% of these HPN patients needed a stoma. The median duration for HPN was 2.5 years. Ten patients had CRBSI. Patients lost weight after 6 months of HPN, which was significant during the first year. The serum concentration of albumin significantly increased during HPN.

In our study, the cumulative incidence of HPN in CD patients was very low. Elriz et al described CD patients with chronic intestinal failure receiving HPN occurring infrequently at French HPN centers, on average 1.9 new cases annually over 21 years.[6] This low incidence in both the studies could be because EN is still considered the mainstay of providing nutrition to CD patients due to its easier availability, maintenance, and cost-effectiveness as compared to parenteral nutrition.[12] Additionally, previous studies of the Olmsted County cohort reported that only approximately 10% of CD patients required 3 or more bowel resections,[20] and that the median cumulative length of bowel resected in the Olmsted County cohort was approximately 60 cm[21]—thus, SBS due to multiple resections is uncommon in the Crohn population.

In our study, the main indications for HPN were SBS and malnutrition. In a single-center experience describing 302 pediatric patients, the main indications for HPN were SBS (47%), obstruction (10%), and diarrhea (11%).[7] Parenteral nutrition is indicated in CD, when it is impossible to provide EN due to SBS, bowel obstruction, ileus, or the presence of

TABLE 2. HPN Indication, Duration, Weight Changes, and Possible Reasons for Changing Weight in Patients With CD Who Required HPN in Olmsted County, Minnesota

Subjects	Duration of HPN (days)	Pre-HPN Weight (kg)	Weight, 6 Months (kg)	Weight, 12 Months (kg)	Weight, 24 Months (kg)	Length of Bowel Remaining (cm)
1	906	56	66.5	65.7	59.2	125 cm SB
2*	3816	45.5	46.3	47.2	48.2	70 cm SB
2*	858	40	44	42.5	42	70 cm SB
3	1987	107	99.3	98	88.5	95 cm SB
4	2229	83.4	73	71.2	73	100 cm SB
5*	662	58.6	63.1	55.7	52	125 cm SB, 45 cm C
5*	3458	52	60	61.5	59.6	96 cm SB, 45 cm C
5*	1490	53	56.5	54	54	80 cm SB, 30 cm C
6	911	44.6	44.2	43.7	49.8	225 cm SB
7	5970	53	54.5	52	52	35 cm SB
8	3135	90.5	84	82.7	86.6	105 cm SB
9	773	41.3	43.5		44.8	
10	728	74.8	64	62.3	70.9	150 cm SB
11	844	56	61.2	59.4	57.2	100 cm SB
12	244	55.2	62.7			220 cm SB
13*	640	67.2	69.2	66	59.9	200 cm SB
13*	254	56	59.8			165 cm SB
14	41	64.5	67			140 cm SB

*Patients required to be on HPN more than 1 time during disease course.
C, colon; SB, small bowel.

TABLE 3. Changes in Laboratory Tests in Patients With CD Who Required HPN in Olmsted County, Minnesota

Laboratory Test	Median (Range) Pre-HPN	Median (Range) at 6th Month	Median (Range) at 12th Month	Median (Range) at 24th Month
1,25-Dihydroxy Vitamin D	18 (8–50)	25.5 (17–70)	33 (21–54)	27 (14–71)
Serum iron	37 (11–88)	59 (17–130)	56 (28–81)	56 (9–132)
Folate	13.4 (3.8–20)	18 (8.5–23)	12.5 (5–25)	18.9 (7.1–2)
Vitamin B12	425.5 (127–1400)	471 (218–812)	459 (216–940)	563 (277–917)
Zinc	0.7 (0.4–1.1)	0.7 (0.6–1.0)	0.9 (0.4–1.1)	1.1 (0.5–1.5)
ESR	15.5 (4–33)	16 (3–56)	17 (2–47)	16 (5–32)
CRP	8.9 (2–149)	3 (0.5–32)	3.8 (2–12.2)	2 (1.1–4)

ESR, erythrocyte sedimentation rate.

severe enterocutaneous or perianal fistulas in order to provide bowel rest.[9]

In our institution's wider experience of 887 adult patients with intestinal failure who required HPN, 56% were able to taper off of HPN. Likewise, in our study, approximately 70% of our patients were able to discontinue HPN.[22]

HPN is not without risk of complications. Catheter infection is the most common side effect of HPN.[22] Our study had 10 patients (71.4%) with at least 1 CRBSI. In a study of 51 patients with intestinal pseudo-obstruction who required HPN, there were 180 CRBSI.[10] In another study describing 302 pediatric patients, 19% of the hospitalizations were due to CRBSI.[7] In a large single-center study, the CRBSI rate was 18% (465 CRBSIs developed in 187 patients out of 1040).[23] The variability of CRBSI risk in different patient populations is potentially due to a number of factors including: type of catheter

used (PICC vs tunneled), number of lumens in the catheter, location of catheter tips, use of antibiotic or ethanol locks, and self-care of the catheter by the patient.[22]

The HPN patients in this study lost an average of 1.4 kg during the first year after the induction of HPN. This could be either due to noncompliance or because of not correctly estimating and delivering adequate calories to increase or sustain goal weights, especially when patients have another concurrent complication like infection. IBD may increase metabolic needs due to the energy consumption by the disease process. This principle was demonstrated in a recent case report where the metabolic needs due to disease process were much higher than equations predicted. The patient was fed 500 kcal in excess of the calculated resting energy expenditure, eventually resulting in its weight gain of 12 kg in 8 months.[11] We can thus surmise that it might be in the benefit of the patient to be given extra calories in order to overcome the calorie deficit due to increased metabolic needs of active CD. Another probable reason for the weight loss could be improvement in Alb level which resulted in mobilization of fluid. Decreased use of corticosteroids could be associated with weight loss as well. Indeed, in 75% of our patients who had persistently declining weight changes, corticosteroids were being tapered. The lifesaving aspects of HPN are often countered by the some of the limitations that patients experience, which can affect quality of life and potentially compliance. On the positive side, it is interesting to note that serum CRP concentrations decreased over time; however, we cannot conclude that the observed decreases in CRP were a direct result of HPN. In a recent systematic review of 15 studies examining the effect of parenteral nutrition on IBD, CD activity scores improved, as did serum albumin, but interestingly, body weight did not change significantly.[24]

Our study had a number of strengths, including the fact that it utilized the REP, which allows access to complete medical records of a population-based cohort of patients diagnosed with CD. In addition the confirmation of diagnosed CD cases on HPN therapy approached 100%. Finally our study represents a well-characterized population-based inception cohort of CD patients on HPN. This stable population is in a defined geographic area over an extended period of time, and is likely representative of the general population. The limitations of our study include that it is a retrospective cohort study, which may miss some data that is not contained in the medical records. In addition, since the majority of the population in Olmsted County is Caucasian (80%), extrapolating the findings to other ethnicities may be problematic. We did not include the patients who required short-term total parenteral nutrition to optimize nutrition status prior to surgery. Finally, our sample size was small, which may under power our study for some detailed and comparative analysis.

In conclusion, only a very small proportion of CD patients need HPN. Our patient population lost an average of 1.4 kg after 12 months of HPN. When deciding to place a CD patient on HPN, providers need to weigh the benefits and risks of HPN and only those who fail conventional therapy with ongoing malnutrition should be considered. CD may be hypermetabolic during active stages of disease and this should be considered if weight loss occurs while on HPN. Due to the small sample size of our study, it is difficult to establish the cumulative incidence and judge the long-term outcomes of HPN in CD patients; therefore, it is required to conduct both retrospective and prospective studies in the future with a larger sample size.

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DATA AVAILABILITY

The data from this study are available upon request from the corresponding author. The data are not publicly available due to information contained within that could compromise the privacy of study subjects.

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