Use of Preoperative Exclusive Total Parenteral Nutrition is associated with Clinical and Laboratory Remission in Severe Active Crohn’s Disease

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Abstract

Background: Crohn’s Disease (CD) patients with active penetrating and stricturing disease have a high prevalence of malnutrition that has been shown to increase post-operative complications. The effect of 1-3 months of pre-operative exclusive Total Parenteral Nutrition (TPN) in active CD patients is not well established. We investigated the efficacy of exclusive TPN in active CD patients.

Methods: From our IBD Center database (prospectively collected data) we identified all patients with complicated, active CD who were candidates for bowel resection between January 2016 and October 2018. CD location and activity were recorded based on the modified Montreal classification. Inclusion required exclusive preoperative home TPN without additional oral intake for 1-3 months prior to surgery. The Harvey Bradshaw Index (HBI), Body Mass Index (BMI), C-Reactive Protein (CRP) and albumin levels were recorded at baseline and at the end of TPN therapy.

Results: Twenty pre-operative CD patients (65% male, 35% female) on exclusive TPN were identified. The mean age of the cohort was 30.75 ± 11.6 years with median disease duration of 8 years (IQR 2.5-11). Mean duration of pre-operative TPN treatment was 73 days (range 24-142 days). Most patients had terminal ileal (35%) or ileocolonic CD (30%), and the stricturing (B2) phenotype was present alone or in combination with other phenotypes in 95% of patients. During TPN therapy, 65% were on stable doses of medication (immunomodulators and/or biologics) and 35% received no medication. All 20 patients had significant clinical improvement in all disease activity indices at the end of preoperative TPN (baseline vs. post TPN): HBI 14.5 vs. 4.0 (p=0.001); BMI 19.2 vs. 19.7 kg/m2 (p=0.017); CRP 57.2 vs. 10.3 mg/L (p=0.001); and albumin 2.7 vs. 3.6 g.dL (p=0.001). Two patients (10%) no longer required bowel resections after completion of exclusive TPN.

Conclusion: Exclusive preoperative TPN was associated with weight gain, decreased inflammatory biomarkers, and improved clinical disease activity and nutrition. While the initial results are promising, further studies are needed before a recommendation can be made to use exclusive preoperative TPN for at least 1 month for severe, refractory CD to decrease disease activity and improve nutritional status before elective surgery.
Introduction

Crohn’s Disease (CD) is a chronic relapsing and remitting autoimmune disease marked by transmural inflammation that most commonly affects the small and large intestines. The incidence of Inflammatory Bowel Disease (IBD) continues to increase across newly industrialized societies, while the prevalence of IBD exceeds 0.3% in North America, Europe and Australia, thus posing a high burden to global health care systems [1]. While the biologic era with anti-TNF therapy has revolutionized IBD treatment, surgery still plays a crucial role in the management of refractory Crohn’s Disease (CD) as a last line therapy, especially in the cases of aggressive penetrating and fibrostenotic phenotypes [2,3]. Approximately 50% of CD patients will require surgery within 10 years of diagnosis, and about 25% of those will require a second intestinal resection within 5 years [4-6]. In the case of CD patients necessitating surgery, adequate nutrition remains a challenge since the degree of malnutrition is affected by the disease severity and duration, and the magnitude of inflammation—which is anorexigenic and thus drives catabolism [7]. Up to 85% of CD surgical candidates are malnourished due to decreased dietary intake and malabsorption as a consequence of active disease [8]. Moreover, malnutrition is a well-known independent risk factor for postoperative complications including infections, poor wound healing and anastomotic leak that may directly lead to increased costs from increased postoperative hospital length of stay and/or reoperation [9-11]. In general, postoperative complications occur in approximately 30% of CD patients undergoing intestinal surgery, leading to an increased burden for patients, physicians and health care systems [12,13]. There are some data to support preoperative nutrition optimization to minimize postoperative morbidity in Gastrointestinal (GI) surgery [10,14,15]. However, there is limited data to support the use of exclusive preoperative Total Parenteral Nutrition (TPN). The purpose of this study is to assess the efficacy of exclusive TPN on nutritional optimization prior to surgery in a CD cohort that failed medical management.

Methods

Study Population

This was an interventional pre-post study of adult patients (age 18-75 years) with endoscopic and histologically confirmed CD with refractory, complicated disease who were bowel resection candidates between January 2016 and October 2018 were identified by our specialist dietician and prospectively enrolled at a single tertiary IBD. Inclusion criteria for preoperative TPN therapy required at least one of the following indicators for malnutrition according to the Malnutrition Universal Screening Tool (MUST): BMI <18.5 kg/m², weight loss >10% within the last 6 months, and/or serum albumin <3 g/dL. In addition, patients were required to complete at least 3 weeks of exclusive preoperative home TPN without additional oral intake. The TPN intervention was initiated in the in-patient setting and continued with home TPN for the remainder of the therapy duration.

Scores

At baseline, the disease location and behavior were recorded based on the modified Montreal classification. Disease location phenotypes include: L1 (terminal ileum); L2 (colon); L3 (ileocolon); and L4 (upper GI), which is subdivided into L4a (proximal to the ligament of Treitz) and L4b (distal to the ligament of Treitz). Disease behavior phenotypes include: B1 (non-stricturing, nonpenetrating); B2 (stricturing/stenotic); B3 (penetrating); and P (perianal disease modifier). The Harvey-Bradshaw index (HBI) is a clinical assessment of Crohn’s disease activity based on five exclusively clinical parameters: 1) patient well-being, 2) abdominal pain, 3) number of liquid or soft stools, 4) abdominal mass and 5) complications. A cumulative score <5 suggests remission, a score between 5 to 7 suggests mild activity, a score between 8 to 16 suggests moderate activity and a score >16 suggests severe activity. C-reactive protein (CRP) is an indicator of systemic inflammation and can be a useful marker to monitor the effect of treatment on systemic inflammation. The laboratory at our institution used a cutoff value > 5 mg/L to define abnormally increased levels. Albumin is a protein synthesized by the liver that can be used as a surrogate marker of nutrition to help assess protein intake. An albumin range between 3.4 to 5.4 g/dL was considered normal by the laboratory at our institution. The body mass index (BMI) is a weight-to-height ratio to determine if a patient is at a healthy weight or not. A BMI score <18.5 is considered underweight, a score between 18.5 to 24.9 is normal, a score between 25 to 29.9 is overweight and a score >30 is obese. The HBI, BMI and albumin were recorded at baseline and after completion of the TPN intervention.

Statistics

Statistical analyses were performed using SPSS version 24.0 software (IBM Corporation, Armonk, NY, USA). Demographic and clinical parameters were evaluated with means and standard deviations or medians and interquartile ranges as indicated. The nonparametric Mann-Whitney U test was performed to compare subgroups since variables were not normally distributed.

Results

Twenty preoperative patients (65% male, 35% female) with refractory CD on exclusive TPN were included (Table 1). The average age of the patients was 30.75 ± 11.6 years, and the median disease duration was 8 years (IQR 2.5-11). Mean duration of TPN treatment was 73 ± 28 days, and every patient completed at least 24 days of exclusive TPN (range 24–142 days). The most common disease locations in our cohort included the terminal ileum (35%), ileocolonic region (30%) and a combination of...
the terminal ileum plus the more proximal small intestine distal to the ligament of Treitz (25%). One patient had CD localized to the colon, while another patient had a combination of colonic CD with small intestinal involvement distal to the ligament of Treitz excluding the terminal ileum (Table 1). Disease behavior of the study population is summarized in Table 1. Nine patients (45%) had the B2 stricturing/stenotic phenotype, which was the most common disease pattern in the study. Nineteen patients (95%) had some degree of stricturing including 20% with penetrating lesions (B3) and 15% with non-penetrating lesions (B1). Perianal disease (P) was present in 20% of patients.

Table 1: Demographics and disease characteristics (n=20).

| Age (years) | 30.75 ± 11.6 |
| Male        | 13 (65%)     |
| Female      | 7 (35%)      |
| Disease Duration (years) | 8 (IQR 2.5-11) |
| Disease Location: |
| L1          | 7 (35%)      |
| L2          | 1 (5%)       |
| L3          | 6 (30%)      |
| L1, L4b     | 5 (25%)      |
| L3, L4b     | 1 (5%)       |
| Disease Behavior: |
| B2          | 9 (45%)      |
| B2, B3      | 3 (15%)      |
| B1, B2      | 4 (20%)      |
| B2, P       | 1 (5%)       |
| B3, P       | 1 (5%)       |
| B1, B2, P   | 1 (5%)       |
| B2, B3, P   | 1 (5%)       |

L1 = terminal ileum; L2 = colon; L3 = ileocolonic; L4b = upper GI distal to ligament of Treitz excluding ileocolonic; B1 = non-structuring, non-penetrating; B2 = structuring/stenotic; B3 = penetrating; P = perianal disease modifier.

All 20 patients in the study demonstrated significant clinical improvement in all disease activity and nutritional indices from baseline to the end of preoperative treatment (Table 2, Figure 1). Overall, there was a significant increase in albumin from a median of 2.7 g/dL to 3.6 g/dL (p=0.001). These results suggest that overall the study population began with inadequate protein intake at baseline-indicated by a low median albumin score (<3.4 g/dL)-and that the protein intake significantly improved by the end of the TPN treatment due to the normal post-treatment albumin level of 3.6 g/dL. The laboratory marker for systemic inflammation CRP significantly decreased from a median of 57.2 mg/L to 10.3 mg/L (p=0.001). Significant increases in weight gain were observed by an overall increase in the median BMI from 19.2 kg/m² to 19.7 kg/m² (p=0.017). Finally, overall clinical improvement in the study population was demonstrated by a significant decrease in the median HBI from 14.5 to 4.0 (p=0.001). This represents a significant decrease in clinical disease activity from moderate disease (HBI score 8-16) to clinical remission (HBI score <5). Interestingly, two patients (10%) no longer required bowel resection after the completion of exclusive TPN due to significant clinical and laboratory remission with concurrent alleviation of symptoms.

Table 2: Outcomes (n=20).

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Baseline</th>
<th>After TPN treatment</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin (g/dL)</td>
<td>2.7 (IQR 2.5-3.4)</td>
<td>3.6 (IQR 3.4-4.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>57.2 (IQR 30.4-110)</td>
<td>10.3 (IQR 5-26.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>19.2 (IQR 17.7-21)</td>
<td>19.7 (IQR 18.9-21.8)</td>
<td>0.017</td>
</tr>
<tr>
<td>HBI</td>
<td>14.5 (IQR 9.7-19.2)</td>
<td>4 (IQR 2-6)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Discussion
Based on our study, exclusive preoperative TPN was
associated with statistically significant weight gain, decreased inflammatory biomarkers, and improved clinical disease activity and nutrition. The significant improvement in the nutritional status in patients with active moderate-to-severe IBD on TPN has been demonstrated in the literature. The BMI increase of 0.5 kg/m² in our study was similarly found in a previous study by Seo, et al. which demonstrated a statistically significant BMI increase of 0.4 kg/m² (p<0.01) in Crohn’s disease patients who received 3 weeks of TPN [16]. Furthermore, several other studies have similarly demonstrated a significant elevation and normalization of serum albumin levels after receiving TPN therapy [17-19]. However, to our knowledge, no prior study has prospectively evaluated the efficacy of home TPN using objective indices of both nutrition and disease activity. The robustness of prospectively collected data on the BMI, serum albumin, serum CRP and the HBI is a major strength of our study. In addition, our team comprised a specially trained IBD dietician who administered the home TPN and accurately recorded weight and nutrition related information on each patient in our database.

While none of the participants in this study developed complications secondary to the exclusive home TPN intervention, the literature reports complication rates as high as 61% [17,20,21]. This includes a Mayo Clinic prospective study conducted between the years 1990 to 2011, which reported a 27% infection rate in IBD patients receiving home TPN for less than 6 months and a 47% infection rate greater than 6 months [20]. In addition to infection including catheter-associated sepsis, other complications reported include blocked or damaged catheters, venous thrombosis, liver failure, dehydration and electrolyte imbalance [21,22]. While the results of this are very encouraging in improving the preoperative nutrition and Crohn’s disease status, there are several limitations. First, both the subjects and researchers were unblinded, which has the potential to introduce bias due to the expectations of disease and nutrition improvement from the exclusive TPN treatment. Second, the small sample size (n=20) limits the statistical power of this study. A larger study in the future may be warranted to further validate the results. Furthermore, an exclusive home TPN regimen of 1-3 months’ duration is very challenging for the patients to strictly adhere to and nearly impossible for the clinical staff to guarantee compliance of the in-home treatment. Additionally, home TPN is expensive. The estimated cost of home TPN was $280 ($238-$390) per day depending on the glucose and lipid content [23]. The high cost of home TPN may be prohibitive to those without health insurance.

Future aims of this study will be to assess the postoperative outcomes of patients preoperatively treated with exclusive TPN matched to standard-of-care controls (i.e. no preoperative exclusive TPN). We hypothesize that patients treated with preoperative exclusive TPN will have improved perioperative outcomes with decreased infections and anastomotic leaks due to a reduction in the preoperative inflammatory burden combined with an increased nutritional status. In summary, Exclusive preoperative TPN was associated with significant weight gain, decreased inflammatory biomarkers, improved nutritional status, and improved clinical disease activity. These data suggest that at least 3 weeks of exclusive TPN are associated with significant improvements in both clinical and laboratory indicators of CD remission.

References


