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Original article

Five-year survival and causes of death in patients on home parenteral nutrition for severe chronic and benign intestinal failure

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SUMMARY

Background & aim: Home parenteral nutrition (HPN) is the primary treatment for chronic intestinal failure (IF). Intestinal transplantation (ITx) is indicated when there is an increased risk of death due to HPN complications or to the underlying disease. Age, pathophysiologic conditions and underlying disease are known predictors of HPN dependency and overall survival. Although the cause of death on HPN is mostly related to underlying disease in these patients, the relationship between mortality and duration of HPN use remains unclear. The purpose of the present study is to describe factors associated with survival and HPN dependency as well as causes of death in adult patients requiring HPN for chronic intestinal failure during the first 5 years of treatment with HPN.

Methods: A multicenter international (European and USA) questionnaire-based retrospective follow-up of a cohort of 472 IF patients who started HPN was conducted between June and December 2000. Study endpoint was either end of 5-year follow-up, weaned-off HPN, ITx, or death on HPN. Data were analyzed for HPN dependence and overall survival using Kaplan–Meier models and log rank tests.

Results: The overall survival probability was 88%, 74% and 64% at 1, 3 and 5 years respectively. Survival was inversely related to age ($p < .001$) and higher in patients with Crohn's disease or chronic idiopathic pseudo-obstruction. A total of 169 (36.5%) patients were weaned-off HPN mainly (80%) within the first year and most frequently in patients with fistulae. Five of the 14 patients who underwent ITx died. By the end of the study, 104 (23%) of patients died on HPN; 65% of deaths occurred within the first 2.5 years of HPN.

Conclusions: Younger ages at HPN initiation and underlying pathologies are significantly predictive of survival on HPN. Risk of death is greatest during the first 2 years of HPN.

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1. Introduction

Intestinal failure (IF) is a highly disabling condition that occurs when gut function is reduced below the minimum necessary for the absorption of macronutrients or water and electrolytes requiring intravenous supplementation to maintain health or growth [1]. IF usually follows major resection of the gut (e.g. short bowel syndrome (SBS)), but can also occur due to trauma, disease, or congenital defect. The most common underlying pathophysiologic conditions leading to IF include Crohn's disease, motility disorders such as chronic intestinal pseudo-obstruction (CIPO), intestinal fistulae, mesenteric vascular disease, radiation enteritis, or infarction [1].

IF can be transient or irreversible, depending on the length of residual small intestine, colon in continuity, nature of the primary disorder and mucosal function of remnant gut. Chronic IF (CIF) is rare with a prevalence of 1–2 per 100,000 and incidence of 1–2 per 1,000,000 [1]. Recently, European Guidelines were developed by the Home Artificial Nutrition & Chronic Intestinal Failure (Special Interest Group of ESPEN). Authors underlined that CIF management requires complex technologies, multidisciplinary and multiprofessional activity, and expertise to care for both the underlying gastrointestinal disease and to provide HPN support [2]. Without specific care including provision of evidence-based therapy according to remnant intestinal absorption, but also prevention of HPN related complications, IF can lead to increasing malnutrition, metabolic complications (dehydration, kidney failure) and even death. The standard choice of therapy is home parenteral nutrition (HPN) [2,3], however long term use is not without risks (e.g. catheter related infections, venous thrombosis and loss of venous access, progressive steatohepatitis and further liver failure, and metabolic bone disease) [2–7]. Hepatic cholestasis and hepatic steatosis are evidence of intestinal failure-associated liver disease (IFALD). In adults, steatosis is more common and found in 40–55% of SBS patients. In adults with IFALD, about 5–15% will develop liver failure [5–7]. Annual incidence of venous thrombosis is around 10%. In a prospective study in HPN patients, the incidence of thrombosis 12 months after catheter insertion was 0,045/catheter/year [2,7]. The gut has an inherent capacity to adapt both functionally and morphologically and enteral autonomy is possible, usually within 2 years and in 50% of cases depending on colon continuity and underlying etiology [8,9].

Intestinal transplantation (ITx) is an alternative life-saving management option for patients at high risk of death due to HPN complications, severe SBS or for those unable to cope with HPN [9–11]. However, despite its relative safety and efficacy, ITx survival still appears to be lower than with HPN [8,12,13]. Previous surveys of patients on long-term HPN have reported survival rates ranging from 70% to 82% in adults and as high as 95% in children after the first 3 years of treatment [14–18]. Surveys indicated that weaning off HPN and mortality rate on HPN were higher during the first years of treatment. Patient's age, cause of IF and underlying disease are prognostic factors for both PN-dependency and patient survival. The causes of death on HPN have also been reported but no relationship with the duration of HPN has been found. However, these studies have been limited to short follow-up periods and have not clearly established a rate of HPN weaning or described causes of death [8,9,14].

The purpose of the present study was to describe the 5-year survival of 472 nonmalignant, non-acquired immunodeficiency syndrome adult patients with chronic benign IF requiring HPN. We also explored causes of death and HPN dependence.

2. Patients and methods

2.1. Study design

A retrospective cohort of 472 consecutive adult patients with benign IF was enrolled from 14 HPN centers (13 European and one US HPN center) between January 1, 2000 and December 31, 2004. Any patient with evidence of a progressive primary malignancy or who were HIV positive at baseline were excluded from the study.

2.2. HPN centers and patient selection

HPN centers in the US and Europe that had previously contributed to surveys initiated by the European Society for Clinical Nutrition and Metabolism (ESPEN) Home Artificial Nutrition (HAN) – Chronic Intestinal Failure (CIF), [ESPEN HAN-CIF] Working Group were invited to participate. Each HPN center received a cover letter describing the study protocol. Fourteen out HPN centers (13 European and one US) agreed to participate.

Structured questionnaires, designed by the members of ESPEN HAN-CIF working group, were distributed to each of the 14 participating HPN centers by the study coordinator (LP) on January of each year of the follow-up. Data were collected over a period of 6 months between June 1 and December 31, 2009 to obtain a maximum of 5 years of follow up on HPN. The questionnaire was completed for each individual patient by the local medical team at the HPN center and returned to the study coordinator for statistical analysis. Patient records were anonymized. The study was conducted with full regard to confidentiality and protection of the individual patient.

Baseline data for each study participant was collected from the patient's medical charts and doctors' notes including: date of HPN initiation, demographic variables (sex and age), diagnosis of primary disease, cause of IF, comorbidities and indication for ITx when present.

The patient's status on December 31 of each year of the follow-up was collected from the patient's charts and reported as: weaned-off HPN (date), currently on HPN, ITx (date and type of transplant), deceased on HPN (date and cause of death), or deceased after ITx (date and cause of death).

2.3. Data management

Patients were grouped into four age categories: 18–30 years, 31–50 years, 50–70 years and over 70 years.

The underlying disease was the disease from which the intestinal failure originated. The principal diseases were; arterial mesenteric ischemia, venous mesenteric ischemia, Crohn's disease, ulcerative colitis, CIPO, Hirschsprung's disease, radiation enteritis, surgical complication, intestinal volvulus, Familial polyposis, necrotizing peritonitis, connectivitis, refractory celiac disease, intestinal epithelial dysplasia, microvillus atrophy, intractable diarrhea on unknown etiology, necrotizing enterocolitis, allergic enteropathy, autoimmune enteropathy and intestinal malformation.

The causes of IF were classified into four pathogenic categories: SBS, chronic motility disorders, intestinal fistulae and extensive small bowel mucosal disease.

Physicians of each center precise on the questionnaire the causes of death (the cause from which the final event originated). A classification was proposed with four categories; 1) HPN-related including CVC-sepsis, CVC-vein thrombosis, liver failure or other

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