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Original article

Survival and nutritional dependence on home parenteral nutrition: Three decades of experience from a single referral centre

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SUMMARY

Background: Home parenteral nutrition (HPN) is the mainstay of treatment for patients with Type 3 intestinal failure (IF), however long term data on mortality and nutritional outcomes are limited.
Objectives: To assess the long-term survival and requirements for ongoing HPN in patients receiving treatment at a UK national referral centre for intestinal failure.
Methods: Patients with IF who received HPN for more than 3 months at this Intestinal Failure Unit between 1978 and 2011 had their clinical records reviewed. SPSS 20 was utilised to perform Cox regression analysis and generate Kaplan Meier curves, with the aim of identifying factors associated with death and the continued need for HPN.
Results: Case notes from 545 patients were reviewed. Overall survival (OS) in patients without malignancy at commencement of IF was 93%, 71%, 59% and 28% at 1, 5, 10 and 20 years after starting treatment. Crohn's disease, mesenteric ischaemia and chronic intestinal pseudo-obstruction were associated with a better OS than scleroderma and radiation enteritis on multivariate analysis. Older age at onset of IF was associated with poor OS, while shorter small bowel length or central line sepsis was not. 15% (25/170) of deaths were due to complications of HPN (central line sepsis = 10, IF-associated liver disease = 15). Continued HPN dependence in survivors was 83%, 63%, 59% and 53% at 1, 5, 10 and 15 years, respectively. Among the 153 patients without malignancy who achieved nutritional independence from HPN, 77 (50.3%) did so after surgical reconstruction of the alimentary tract (HPN duration mean 19 months, range 3–126 months). 76 patients (49.7%) weaned from HPN without undergoing surgical reconstruction.
Conclusion: This is the largest reported data set on long-term survival and dependence on HPN and will inform the indications, benefits and risks of treatment in disease specific groups. A significant proportion of patients achieved nutritional autonomy without surgical intervention.

1. Introduction

Home parenteral nutrition (HPN) is the standard treatment for patients with Type 3 intestinal failure (IF) requiring long term support, in whom the functioning gut mass is inadequate to allow sufficient nutrient, water or electrolyte absorption to meet metabolic requirements [1]. Since its introduction in the second half of the 20th century, HPN provision has dramatically improved the prognosis of patients with severe intestinal failure [2,3]. Unfortunately HPN provision is associated with a range of complications, notably catheter-related blood stream infection (CRBSI) and intestinal-failure associated liver disease (IFALD) [4,5], as well as complications relating to the patient's underlying condition. Retrospective cohort studies have reported 5-year survival rates on HPN of between 58% and 83% [3,6,6–9]. Additional larger and longer series to those already published in the literature can add to the evolving understanding of current long-term outcomes in this patient group.

An additional important issue in HPN is the potential for adaptation of small bowel function over time, allowing a degree of weaning from parenteral nutrition in a proportion of patients [8].

Abbreviations: CRBSI, catheter related bloodstream infection; HPN, home parenteral nutrition; CVC, central venous catheter; OS, overall survival; IFALD, intestinal failure associated liver disease; IFU, intestinal failure unit; CIPO, chronic intestinal pseudo-obstruction; ECF, Enterocutaneous fistulae; SBS, short bowel syndrome.

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While such adaptation has previously been thought to occur only over the first two years following onset of intestinal failure [8,10], recent European data suggests that HPN discontinuation is possible up to 5 years following intestinal failure onset and that this is independent of surgical reconstruction [6]. There is sparse data on the potential for adaptation beyond this time point.

We therefore report the largest single-centre series of adult patients requiring HPN over a 33-year period up until 2012 to better define predictors of overall survival and assess the overall chance of achieving nutritional autonomy.

2. Methods

2.1. Study cohort

Clinical records of adult patients receiving home parenteral nutrition (HPN) at Salford Royal Hospital, a national intestinal failure unit (IFU) in the U.K., over a 33-year period between January 1978 and December 2011 were reviewed. Patients were identified from a prospectively maintained database. Patients had to be prescribed calorie-containing fluids (not electrolytes only) at least one night per week for a duration of at least 3 months to be included in this study. The censoring date was the 11th December 2011. We estimate that the final data set collected represents 94% of all HPN patients at Salford Royal Hospital based on internal validation of a subset of 580 patients. Patients excluded due to missing data primarily received HPN in the 1980s, as records at that time were paper-based and many have since been destroyed or archived. Patients receiving HPN for a diagnosis of palliative cancer were excluded from survival analysis but otherwise included in the study.

2.2. Study protocol

The majority of patients were managed with single-lumen tunnelled central venous catheters and HPN was delivered using a stringent catheter care protocol either by the patients, their relatives and trained nursing staff using a standardised protocol in accordance with ESPEN guidance [11]. PN was prepared by commercial providers in an aseptic facility. Patients were either rigorously trained to deliver the PN themselves or were supported by relatives or trained nursing staff. Patients and caregivers were regularly reassessed to ensure appropriate use of the protocol. Patients were given the minimum number of nights PN to meet their nutritional needs and encouraged to have oral and/or enteral nutrition if able. Where possible, parenteral lipids were delivered once or twice per week and lipid dosing was limited to 1 g/kg/day. All patients were reviewed regularly in the clinic and the HPN content and volume optimized according to on-going requirements.

2.3. Data collection

Data collected included gender, age at start of HPN, primary diagnosis, mechanism of IF and duration of treatment. Primary diagnoses were classified as surgical complication, Crohn's disease, mesenteric ischaemia, chronic intestinal pseudo-obstruction (CIPO), radiation enteritis, volvulus, congenital, scleroderma, FAP/desmoid or 'other'. Patients with Crohn's disease who developed IF as a consequence of complications of surgery were included in the Crohn's disease group rather than the surgical complications group. Furthermore, the mechanism of IF was classified as short bowel syndrome, SBS with enterocutaneous fistula (ECF), ECF, pseudo-obstruction, mechanical obstruction or malabsorption. Patient survival, including details of the cause of death, was recorded. Catheter-related blood stream infections (CRBSI) were strictly diagnosed using standard criteria and recorded from 1993; infection rates were therefore calculated from this time point. Diagnosis of a CRBSI from 1993 was based on quantitative and qualitative assessment of central and peripheral blood cultures and pour plates as per ESPEN guidelines [11]. Anatomical characteristics including small bowel length in continuity (assessed either at surgery or radiologically as appropriate), presence or absence of colon and whether the colon was in continuity along with details of any intestinal stomas were recorded. The need for on-going HPN at the date of censoring, details of any intestinal reconstructive surgery undertaken and nutritional outcome (oral/enteral) were also recorded. Dependence on long-acting opiates was also recorded although this data was only available in detail from 2003.

2.4. Statistical analysis

Data are presented as means ± SD or medians (range) as appropriate. Statistical analysis was performed by using the SPSS software package (version 22.0; SPSS Inc. Delaware, USA). Student T-tests and one-way Anova with Bonferroni corrections were used for parametric data and the Mann–Whitney U was used for non-parametric data. Kaplan–Meier curves were generated and the Log-Rank test used to identity differences between groups. Significance was taken as $P < 0.05$. Cox regression was performed to assess prognostic factors related to time of death from any cause among the patients without underlying malignancy. CRBSI were treated as a time-dependent co-variate. In the univariate analysis, gender; age; primary diagnosis; mechanism of intestinal failure; small bowel length; presence of a duodenostomy, jejunostomy or ileostomy; presence of colon in (continuous) or out of continuity (discontinuous) with the rest of the gastrointestinal tract; CRBSI; decade of commencing HPN were analysed. Factors that demonstrated an effect upon survival of greater than 0.2 were included in the multivariate analysis. A second descending stepwise Cox regression model was developed to identify independent prognostic risk factors. Furthermore, trends over time were analysed by comparing three time periods chosen to include an equal number of patients commenced on HPN over the 33-year period.

3. Results

3.1. Patient characteristics

Details relating to 545 patients were available for review representing 2330 patient-years of HPN provision (Table 1). The median (range) duration of follow-up was 25 (range 3–351) months. The primary diagnoses and mechanism of intestinal failure are detailed in Table 1. Gastro-intestinal anatomy is also described in Table 1. 88 patients underwent a planned reconstructive surgical procedure aimed at restoration of intestinal continuity during the period of the study.

Changes in the prevalence of underlying diagnoses and mechanism of IF over time are demonstrated in Table 2. There has been a reduction in the prevalence of Crohn's disease among patients receiving HPN (81/170 (48%)) in 1978–1998 to 40/179 (22%) in 2006–2011 while the prevalence of active malignancy increased.

3.2. Survival and complications of HPN

There were 171 deaths in total in the cohort during the study period (Fig. 1). During the first two years of HPN treatment, the majority of the deaths were either related to underlying primary benign disease, pre-existing malignancy or sepsis (Table 3). Patients were most likely to die from sepsis followed by co-morbidities and

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