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ABSTRACT

Objectives, setting and patients: With complete case referral for prolonged parenteral nutrition (PN) beyond term equivalent, serving a stable population of 1.25 million people, we describe the long-term outcome and survival of patients referred to an intestinal failure (IF) nutrition support team over the first 8 years of existence at a regional paediatric centre, and extrapolate to potential numbers of national home parenteral nutrition (HPN) cases and intestinal transplantation data.

Design and outcome measures: Retrospective analysis detailing patient demographics, interventions, use of HPN, occurrence of intestinal failure-associated liver disease (IFALD), and outcomes of enteral adaptation, survival, and referral for and receipt of organ transplantation.

Results: 23 patients were referred over 8 years, 20 being PN dependent within the neonatal period. Diagnoses included short bowel syndrome (SBS) (18), neuromuscular abnormalities (4) and congenital enterocyte disorder (1). 12 696 days of PN were delivered with 314 confirmed episodes of sepsis at a median of 12 episodes per patient. 144 central venous catheters (CVCs) were required at a median of four per patient. IFALD occurred in 17 (73%) patients, with 10 (44%) referred for transplant assessment. Thirteen (56%) children received HPN. Overall mortality was 44%. A significant predictor for survival in the SBS group was residual bowel >40 cm (82% vs 28%, $p = 0.049$).

Conclusions: Survival for IF at 56% was lower than reported from non-UK supra-regional centres, and nationally collected data, possibly reflecting pre-selected referral populations. Data from regional centres with complete ascertainment may be important both when counselling parents and when planning regional and national HPN and IF specialist services.

What is already known on this topic

- The prevalence of intestinal failure is rising and long-term survival of home parenteral nutrition patients from some national centres has risen to >90% in recent years
- Intestinal failure-associated liver disease contributes significantly to long-term morbidity and mortality of these patients.

What this study adds

- Outcomes from these regional data are poorer than previously described national data; this may reflect a fuller ascertainment and thus a greater burden of disease than currently recognised.
- Regionally obtained data suggest an underestimate in national resource requirements for home parenteral nutrition and combined small bowel and liver transplantation or isolated liver transplant services.

Intestinal failure (IF) is defined as the reduction of functional gastrointestinal mass below that needed for digestion and absorption of fluid and nutrients for maintenance in adults and growth in children.[1–3] It can be separated into three main groups by pathogenesis.[4 5] These are: (1) short bowel syndrome (SBS)[6]; (2) neuromuscular disorders of the gastrointestinal tract including long segment aganglionosis (Hirschsprung's disease) and congenital intestinal pseudo-obstruction syndromes (CIPOS)[7]; and (3) congenital enterocyte disorders.[8 9] Parenteral nutrition (PN) has dramatically improved the previously dismal prognosis for this patient population.[1 5 10] However, significant complications of management, such as central line sepsis, intestinal failure-associated liver disease (IFALD) and growth failure, have contributed to long-term morbidity and mortality in IF.[1 5 11] Combined small bowel and liver transplantation (CSBLT) now offers alternative treatment for patients surviving with irreversible IF.[5 12] Currently, care for IF in the UK is performed in regional paediatric gastroenterology and nutrition services with multidisciplinary nutrition support teams (NSTs).[13] At the time of writing, there is a single intestinal transplantation unit located at Birmingham Children's Hospital. Outside the UK, national centres of excellence for management of long-term IF and home parenteral nutrition (HPN) exist.[14] Outcomes for patients with longstanding IF appear to be improving, as seen from data collected from national centres of excellence (outside the UK) and from intestinal transplantation services.[14 15] However, there is a paucity of incidence and outcome data for such patients from regional centres. This study aimed to describe the incidence, prevalence and long-term outcome of IF referred to a regional NST, when all cases from a geographical region are obtained, and to extrapolate these data for potential use of national HPN and intestinal transplant services.

METHODS

Setting and patients

Following the appointment of a consultant in paediatric gastroenterology and nutrition in

August 1997, the Royal Hospital for Sick Children, Edinburgh (RHSC) developed a multidisciplinary IF NST. This consisted of a consultant paediatric gastroenterologist, consultant paediatric surgeons, specialist paediatric nutrition nurse, paediatric dieticians, specialist paediatric pharmacist, ward nursing staff, and specialist social worker. The RHSC serves as the single tertiary paediatric unit to the region of southeast Scotland with a stable population of around 1.25 million, and provides all PN to post-term infants and children. Referral to the team is made from within the RHSC (medical or surgical teams), from four other district general paediatric units, two level three NICU and two level two neonatal nurseries within the region. The aims of the team were to optimise the long-term outcome of patients identified as having IF by maximising enteral nutrition, facilitating the use of HPN and acting as a point of referral to UK national transplantation services when required.

In-patients are managed in a combined medical and surgical ward and are reviewed by the multidisciplinary ward-round on a daily basis with alterations to therapies and PN being made to optimise bowel adaptation. PN prescription is conducted in conjunction with a senior specialist paediatric pharmacist. Central lines are placed and removed by paediatric surgeons dedicated to the NST. Training and supervision of line-care by ward staff, junior doctors and parents is coordinated by a dedicated nutrition nurse specialist. PN is always cycled to an optimal level dependent upon age, prematurity and clinical status. Enteral feeding is modified by the NST specialist paediatric dietician. As a rule, when available, the mother's milk is the first feed. When not tolerated, a semi-elemental feed is normally trialled, followed if necessary, by a completely elemental diet. Feeds high in medium-chain triglycerides are given when a patient is significantly cholestatic. Modular feeds are reserved for patients with specific indications, such as suggestion of very low threshold of carbohydrate tolerance. Bilirubin, liver enzymes and synthetic function are assessed weekly with micronutrient nutritional screening on a monthly basis. When IFALD is identified, management involves a protocol of investigation for other causes of cholestatic liver disease, a review of enteral and parenteral nutrition and commencement of ursodeoxycholic acid. A standard sepsis protocol of broad-spectrum antibiotics for fever >38.5°C or recurrent fever >38.0°C exists. Individual patient sepsis protocols are established in conjunction with a specialist consultant microbiologist and are available on the front of patients' case notes. The specialist nutrition nurse trains parents to handle PN and the dedicated social worker identifies and rectifies non-medical hindrances to discharge. HPN patients are discussed in a multidisciplinary meeting weekly, with emphasis being placed on optimising enteral nutrition, sepsis prevention and management and quality of life issues. Patients are seen in a dedicated IF clinic after discharge. We work within the Scottish HPN-managed clinical network (http://www.shpnmcn.scot.nhs.uk) which aims to facilitate excellence and standardisation of care for all HPN patients across Scotland.

Design and outcome measures

Data were obtained retrospectively from the medical records of patients from the IF NST database, logged prospectively from August 1997 to June 2005. These data were analysed by database Excel for Windows (Microsoft Office XP). Entry criteria were patients referred to the regional paediatric NST with a primary gastrointestinal disorder, and who must have received >28 days' PN by completion of study. Demographic data obtained for patients at point of referral to the team were date of birth, age at referral, birth weight, gestational age at birth, diagnoses, weight at referral and number of days of PN at referral. Patients were grouped according to cause of IF – SBS, neuromuscular disease or enterocyte disorder.

SBS patients had additional data recorded for primary diagnosis. Initial surgical records were reviewed and residual small bowel length recorded. Where only length of bowel resected was recorded, an estimated residual bowel length was calculated using a standardised formula against gestation.[16] Other surgical details recorded were: primary anastomoses, defunctioning stomas, and whether the ileo-caecal valve (ICV) had been removed. Patients with neuromuscular disease had primary diagnosis and subsequent surgical procedures noted. Longitudinal data were then obtained to evaluate patient management and outcomes in the following categories.

1. PN and enteral adaptation

Recorded items were the total number of days of PN, total number of semi-permanent tunnelled central venous catheters (CVCs) required and other complications of PN (line occlusion, thrombosis, growth failure, pubertal delay, IFALD), proportion of patients who received HPN, and the number of confirmed episodes of bacterial/fungal sepsis (defined as clinical signs of sepsis in combination with a significant growth of appropriate organism from CVC culture, peripheral line culture or peripheral venous culture, with resolution of symptoms with appropriate antibiotic therapy). Further cultures of the same organism were not considered to be a separate septic episode until the patient had remained afebrile for 5 days off antibiotic treatment. We defined enteral adaptation as <10% weight loss after cessation of PN followed by sustained weight gain. Time to adaptation was recorded in months, and enteral feed regimen at time of adaptation was also recorded.

2. IFALD, transplantation and outcome

Patients were defined as having IFALD (direct bilirubin >50 μmol/l)[17] or being severely cholestatic (direct bilirubin >100 μmol/l) either at referral or during their course of treatment. Criteria for referral to the intestinal transplantation unit were conjugated bilirubin >150 μmol/l outwith septic episodes, or progressive fibrotic liver disease on biopsy, lack of vascular access, poor long-term prognosis or very impaired quality of life for parents/carers or patients. We noted whether patients required referral for assessment for CSBLT or isolated liver transplant (ILT) and if they received this assessment, we also noted whether patients were then listed for transplantation, and if so, whether they received transplantation. All transplantation and transplant assessment was performed at the UK supra-regional Intestinal Transplant Assessment Centre at Birmingham Children's Hospital, Birmingham, UK. Outcome data recorded included patient survival, death, age at death, cause of death and death while awaiting organ transplantation.

3. Extrapolation of regional results to national situation

To determine how our data would translate into national statistics, we calculated our service population to be 2.1% of the UK (1.25/60 million × 100%). We then extrapolated what annual registration of HPN patient, annual referral to the intestinal transplantation unit, CSBLT and ILT would be based on these figures ((n×100/2.1)/8 years). We compared our figures with current published UK data on paediatric HPN registration[18] and referral to the intestinal transplantation unit.[15]

Normally distributed continuous data are described as mean (SD), non-normally distributed continuous data are described as median (range), and categorical data are described as number (%). All statistical analyses were performed using Minitab V.14 (Microsoft Office XP) and a p value of $\leqslant 0.05$ was considered significant. Ethical approval is not required for this type of study, confirmed by correspondence with our Local Research Ethics Committee.

RESULTS

Twenty-three patients were referred to the team (18 SBS, 4 neuromuscular disorders, 1 epithelial disorder). Patients referred had a median gestation of 35 weeks (range 25–38 weeks), birth weight of 2.44 kg (range 0.65–3.55 kg), and were referred at a median age of 2 months (7 days–81 months) having received 35 days' PN (0–370 days), respectively. (Patient histories are available as a supplemental file.) Some variability existed in time to referral as a small proportion of patients were already established on PN before the creation of the NST. Patient demographics are summarised in table 1. Out of the SBS cohort, seven (39%) had residual bowel length <40 cm, with eight (44%) having had their ICV removed.

1. PN, sepsis, HPN and adaptation

Twelve thousand six hundred and ninety-six patient days of PN were delivered at a median of 310 days per patient (range 58–2730 days). Thirteen (56%) patients received HPN. There were no significant differences in demographic details between these patients and those in whom adaptation occurred prior to discharge from hospital. There were 314 confirmed episodes of bacterial sepsis (median of 12 episodes per patient (2–52)) at a mean of one septic episode per 40.4 patient days. Bacterial and fungal growths identified in blood culture are summarised in table 2.

A total of 144 CVCs were placed (median four per patient (range 1–24)). Thirteen of 23 patients received HPN. Patients who achieved HPN had a significantly lower infection rate in comparison to those who received all PN in the hospital (1 infection per 45.1 PN days vs 1 per 30.2 PN days, $p = 0.023$, 95% CI −27.6 to −2.3). CVCs lasted a mean of 80.6 patient days, and only five CVCs (3%) were removed because of total line occlusion. We identified three major thrombotic complications (one right internal jugular thrombosis, one bilateral iliac, and one vena cava right atrial). No patients were referred for transplant assessment because of loss of vascular access. Only 10 (44%) patients achieved full enteral adaptation, two of these being post-CSBLT and one post-ILT. Adaptation was achieved at a median of 31 months (range 9–47 months).

2. IFALD, organ transplant and outcome

Nine (39%) patients had IFALD at referral with six (27%) having severe cholestasis. Of the SBS cohort, eight (44%) cases had already developed IFALD at time of referral with six (33%) being severely cholestatic. Seventeen (73%) patients developed cholestasis during the study. Early age of referral to the NST (<3/12) and frequent episodes of infection (<30 days) positively correlated with subsequent IFALD development (table 3).

Twelve (52%) patients developed cholestasis reaching levels which indicated need for referral to the intestinal transplantation unit in Birmingham for assessment (total bilirubin consistently >150 μmol/l outwith septic episodes). Ten were assessed; one family declined assessment and another patient

Table 1 Demographic data of 23 intestinal failure patients referred over 8 years

Patient	Diagnosis	Gestation (weeks)	Birth weight (kg)	Age referral (months)	No of days' PN	Cholestatic
Patient 1	SBS (NEC)	28	0.65	1	36	No
Patient 2	SBS (gastroschisis)	36	2.75	3	75	Yes
Patient 3	SBS (NEC)	31	1.38	1	35	Yes
Patient 4	SBS (NEC)	38	2.30	13	370	Yes
Patient 5	SBS (NEC)	32	1.73	21	210	No
Patient 6	Long segment Hirschsprung's	39	2.78	16	0	No
Patient 7	SBS (NEC)	30	1500	4	14	No
Patient 8	Congenital enterocyte disorder	40	3.98	<1	0	No
Patient 9	Long segment Hirschsprung's	38	3.91	3	0	No
Patient 10	SBS (NEC)	33	2.1	2	45	Yes
Patient 11	SBS (SMA thrombosis)	37	3.0	6	0	No
Patient 12	CIPOS	39	3.21	81	0	No
Patient 13	SBS (NEC)	25	0.86	3	90	Yes
Patient 14	SBS (ileal atresia)	35	2.68	<1	21	No
Patient 15	SBS (gastroschisis)	36	2.44	<1	3	No
Patient 16	SBS (NEC)	25	0.85	3	55	Yes
Patient 17	SBS (NEC)	29	1.7	2	46	Yes
Patient 18	CIPOS	36	4.1	2	50	Yes
Patient 19	SBS (ileo-jejunal atresia)	36	3.55	2	21	No
Patient 20	SBS (NEC)	30	1.68	4	45	No
Patient 21	SBS (ileal atresia)	35	2.8	<1	0	No
Patient 22	SBS (meconium ileus)	39	2.8	<1	12	No
Patient 23	SBS (NEC)	29	1.18	1	43	Yes

Cholestasis was defined as serum bilirubin >30 μmol/l. Patients were referred before commencing PN (ie, were commenced on PN by the nutrition support team).
CIPOS, congenital intestinal pseudo-obstruction syndromes; NEC, necrotising enterocolitis; PN, parenteral nutrition; SBS, short bowel syndrome; SMA, superior mesenteric artery.

Table 2 314 positive cultures from central lines from 23 intestinal failure patients receiving parenteral nutrition

	Positive cultures (%)
Coagulase-negative staphylococcus	145 (43)
Enterococcus faecalis	43 (12)
Klebsiella	36 (11)
Enterobacter cloacae	35 (11)
Escherichia coli	18 (5)
Candida	15 (4)
Staphylococcus aureus	12 (3)
Streptococcus	11 (3)
Pseudomonas	10 (3)
Other	11 (3)

died whilst awaiting assessment. Five (22%) patients received transplants (four CSBLT, one ILT) and two patients died whilst awaiting transplantation. Three remained on the transplant list at the close of audit. In total, 10 (44%) patients died. Causes of death included end-stage liver disease,[4] sepsis,[2] gastrointestinal haemorrhage, post-transplant multi-organ failure, renal failure and cytomegalovirus encephalopathy post-transplant. Median age of death was 12 months (range 7–107). Significant predictors for survival in the SBS group were residual bowel length >40 cm (82% vs 28%, p = 0.049), >3 months' age at referral to NST (81% vs 33%, p = 0.036) and proceeding to HPN (77% vs 30%, p = 0.04) (table 4).

3. Extrapolation of regional results to national situation

We calculated that our total 8-year caseload of 23 patients, 13 HPN patients and 12 patients with indications for referral to transplantation services extrapolate to 1095, 619 and 571, respectively, nationally over 8 years. Ten (77%) of our HPN patients had SBS in comparison with the national average of 40%.[18] Eleven out of 12 (92%) of our patients indicated for referral to transplantation services and 9/10 (90%) of patients referred had SBS, compared with 89/159 (55%) in the intestinal transplantation unit.[15] Our extrapolated annual national registration of HPN patients of 77.4 compares with 14.8 (89/6 years) from the BANS report 2000–2005[18] and our annual rate of referral to the intestinal transplantation unit of 71.4 compares with 17.3 (104/6 years) actual referrals to the intestinal transplantation unit[15] (fig 1).

DISCUSSION

IF in the paediatric population now appears to have a better prognosis in comparison with adults,[14 19] with a greater proportion of patients achieving complete enteral adaptation over time. PN and HPN are the mainstays of medical therapy whilst awaiting this adaptation process. Most reviewers relate increased survival to improved safety of delivery of PN, development of NST and earlier identification of patients with irreversible disease or complications such as IFALD that require referral to transplant services.

On initial reflection our data relating to sepsis rate (1 per 40.4 patient days), severe IFALD (52%), and survival rate (56%) over 8 years represent disappointing outcomes in comparison with other published work.[14 15] However, this may be partially attributable to variations in reporting in terms of definition of IF, and our local case mix. This may then have secondary effects on complications of IF treatment such as sepsis and development of IFALD. IF has been defined in paediatric surveys as any patient requiring PN for >28 days. Other case series have included patients without primary intestinal disorders (including oncology and intensive care patients requiring PN support during prolonged courses of inpatient illness), or patients who have not required PN beyond term.[20] HPN is not an issue for these patients, and they are not candidates for CSBLT. Data gathered from national centres outside the UK may reflect a preselected group that has demonstrated stability on PN for a period of time, and thus produces a referral bias which can lead to improved long-term outcomes.[1 15] Other regions may also have patients with IF being managed beyond term by a service that would not fulfil the criteria for NST. Our institution serves a region with a population of 1.25 million; it has a unique service organisation. As the only centre performing neonatal surgery for the region, with a single NICU providing PN after term, and a single NST, we are confident that we have complete early ascertainment of patients with primary intestinal disorders who have a potential requirement for PN beyond term (as well as all of the older infants, children and teenagers requiring PN). These neonatal patients are those who are likely to require tertiary NST services, as they are the patients who have the potential to receive HPN and/or require referral to transplant services.

PN, HPN and adaptation

We reported on over 12 000 patient days of PN with 56% of patients receiving HPN. Koglmeier *et al*[20] found that only 5% of IF patients required HPN over 2 years. This difference may in part be attributed to disease severity in our patients. Only 44% of our patients achieved enteral adaptation (not all of these patients required specialist NST input). Factors shown to predict time to enteral adaptation in SBS include length of remaining small bowel; a length of ⩾40 cm has been shown to be a significant factor for earlier adaptation.[10] The loss of the ICV, intestinal inflammation and bacterial overgrowth also appear to negatively affect adaptation.[21] The primary stimulus for the bowel adaptation process is enteral nutrition, with early postoperative feeding predicting shortened period of dependency on PN.[22] Other studies have reported marked success in weaning long-term PN patients when instituting an intestinal rehabilitation programme with Torres *et al*[23] achieving 31/37 HPN patients weaning successfully. This figure falls to 64% when dealing with neonatal onset diseases as described by Diamond *et al*.[24] However, the effects of prematurity on outcome are not described in either cohort.

Table 3 Intestinal failure-associated liver disease (IFALD) development according to patient characteristics

Comparator	IFALD development (%)	Significance
NEC vs non-NEC	7/11 (64%) vs 9/12 (75%)	p = 0.667
Age <3/12 vs ⩾3/12 at referral	11/11 (100%) vs 5/12 (42%)	p = 0.005
Infection rate <30 days vs ⩾30 days	9/9 (100%) vs 8/15 (53%)	p = 0.022
Preterm vs non-preterm	13/15 (86%) vs 5/8 (63%)	p = 0.297

NEC, necrotising enterocolitis.

Table 4 Outcome statistics according to patient characteristics

Comparator	Survival (%)	Significance
NEC vs non-NEC	8/11 (73%) vs 4/12 (34%)	p = 1.000
Age <3/12 vs ⩾3/12 at referral	4/12 (33%) vs 9/11 (81%)	p = 0.036
Preterm vs non-preterm	9/15 (60%) vs 4/8 (50%)	p = 0.685
HPN vs non-HPN	10/13 (77%) vs 3/10 (30%)	p = 0.040
Cholestatic vs non-cholestatic at referral	8/14 (57%) vs 5/9 (55%)	p = 1.000
Residual bowel length ⩾40 cm vs <40 cm	9/11 (82%) vs 2/7 (28%)	p = 0.049
ICV intact vs ICV removal	6/10 (60%) vs 5/8 (63%)	p = 1.000
Infection rate <30 days vs ⩾30 days	2/9 (22%) vs 10/15 (66%)	p = 0.089

HPN, home parenteral nutrition; ICV, ileo-caecal valve; NEC, necrotising enterocolitis.

Sepsis rates and IFALD

We report a high incidence of bacterial sepsis with a median of 12 episodes of sepsis per patient at a rate of one per 40.4 catheter days. Clear guidance for the use of long-term CVC for PN delivery now exists for paediatric patients; the use of dedicated single lumen subclavian catheters is recommended.[25] A dramatic reduction in bacterial sepsis rates has been shown to be associated with both non-touch sterile access of catheters, and having a dedicated PN nurse formally training all ward staff, medical staff and parents on how to access CVC.[25 26] Despite early institution of these measures our sepsis rate remains higher than other series; however, the definition of septic episodes in the literature is often unclear[27–29] and there is a lack of a standardised method of reporting.

In our series 73% of 23 patients developed IFALD and 52% had indications for referral for transplant assessment. The relationship between IF, PN and cholestasis is not clear. Although individual constituents of PN have been shown to be hepatotoxic,[11 30 31] IFALD itself has a multifactorial aetiology. Patients who are able to take some of their nutrition enterally appear to have partial protection from IFALD in comparison with patients who receive all their calories intravenously.[22 32] In addition, a normal functioning small bowel would appear to protect adult populations against cholestasis when receiving PN.[33] Recurrent bacterial sepsis has been heavily implicated in the development of IFALD in neonates and children.[11] Colomb *et al*[34] reported a much lower rate of 23% IFALD in HPN patients, although the proportion of patients who were term or older children was greater in this cohort. Koglmeier *et al*[20] reported that IFALD complicated 59% of paediatric cases of IF. Sondheimer *et al*[35] reported a similar incidence of IFALD (67%) in a series of 42 patients with SBS, and only 17% of these patients went on to develop liver failure. Our criteria for transplant assessment are mostly based on serum bilirubin rather than synthetic liver function, thus making direct comparison of results inappropriate. Fifty-two per cent of patients had indications for transplant assessment, 22% of our patients received organ transplantation, and a further two patients died on the transplant waiting list. This exceeds the previously described figure of 15–20% requiring transplantation.[1] This may partly be a reflection of the severity of disease in our cohort and also the relatively high incidence of bacterial sepsis predisposing to IFALD development. In our series, 48% of detected organisms on blood culture were found to be either Gram negative or fungal, both of which are strong predictors for IFALD development.[35] We suggest that there is a greater burden of liver disease if all IF patients in a geographical area are ascertained, rather than the lesser burden suggested by either nationally gathered data[18] or data from a single or small number of centralised national referral centres.[14 15]

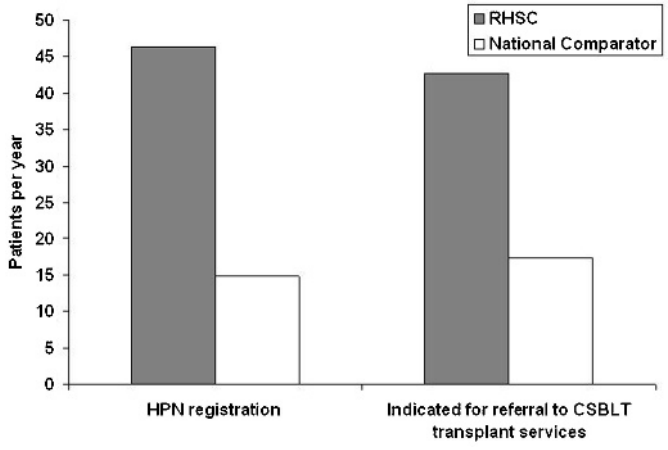

Figure 1 Comparison of Royal Hospital for Sick Children, Edinburgh (RHSC) regional data and extrapolation to national situation in terms of home parenteral nutrition (HPN) registration[18] and indication for referral to combined small bowel and liver transplantation (CSBLT) services[15] expressed as patients per year.

Outcome

We report only 56% survival over 8 years which is lower than other recent studies. Diamond *et al*[24] reported 62.5% over 3 years in an SBS cohort, Colomb *et al*[34] reported 81% survival over 10 years in a paediatric HPN cohort, and Koglmeier *et al*[20] reported 94% survival over 2 years in a paediatric IF series. We would, however, again suggest that the differences in patient ascertainment and patient mix, namely high rates of early referral, prematurity and NEC (48% of our cohort had NEC as opposed to 24–30.8% in other paediatric IF populations[20 36]), may in part explain this low survival rate although numbers of patients are admittedly small. It is of note that of our population referred to the NST very early (<3 months of age), primarily because of early-onset cholestasis, have a particularly poor prognosis (survival 33% compared with 88% if ⩾3 months) and would have been omitted from other published cohorts of this condition (table 3).[14] The 88% survival rate of those infants referred at or after 3 months of age is comparable to the survival data reported from large single-centre HPN programmes, such as the 81% survival rate in 302 patients reported from Paris.[34]

CONCLUSIONS

The economic impact of HPN for paediatric patients is high.[37] The cost-effectiveness of CSBLT versus long-term HPN is not clear,[38] and is a somewhat artificial argument in light of donor organ shortage for the paediatric population. Local factors (high incidence of NEC) may contribute to our high use of HPN. The

registration of paediatric HPN to the BANS registry is not compulsory and therefore these data are likely to be incomplete. However, the great excess in our series of HPN usage and indications for CSBLT services, compared with nationally collected data[15 18] strongly suggest that, nationally, patients may be lost due to early death, discontinuation of care, or non-referral, prior to reaching regional paediatric gastroenterology services, let alone transplantation services. Outcomes data are vital for service planning, but must reflect the full spectrum of the clinical arena; we suggest that with firmer establishment of managed clinical networks for paediatric nutrition support, that the patterns of care for IF patients in the UK will increasingly mirror the current practice in our region in terms of ascertainment and outcomes, with full referral of all cases of IF from early neonatal life. Such data may be of importance both when counselling parents and for future planning of regional IF and national transplant services. Our data also suggest there may be greater need for ILT and CSBLT assessment than currently recognised, and we suggest that the ongoing further national surveillance of IF may clarify the current position (BIFS study http://bspghan.org.uk/working_groups/nutrition.shtml).

The treatment of IF in the paediatric population remains a therapeutic challenge for the future. These patients have highly specialised needs, best served by tertiary care units where sufficient surgical, medical, dietetic and nursing expertise for their management can be developed yet delivered closer to home. Overall throughput is low in terms of numbers, even in large centres. This makes randomised controlled trials of therapies difficult to organise in terms of feasibility. In the absence of a robust evidence base, standardisation of care with clinical guidelines for PN usage[22] together with dissemination of skills through managed clinical networks are the best current ways to optimise care. Close working relationships between regional tertiary units and the central transplant centres is of particular importance. Patient populations in the regional centres may differ from the experience of intestinal transplantation units; sharing and honest appraisal of patient outcomes between regional and intestinal transplantation centres may also help the counselling of parents, regional and national service planning for both HPN and intestinal transplant services, and long-term outcomes for these patients within the UK.

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REFERENCES

1. **Goulet O,** Ruemmele F, Lacaille F, *et al*. Irreversible intestinal failure. *J Pediatr Gastroenterol Nutr* 2004;**38**:250–69.
2. **Gupte GL,** Beath SV, Kelly DA, *et al*. Current issues in the management of intestinal failure. *Arch Dis Child* 2006;**91**:259–64.
3. **Nightingale JM.** Management of patients with a short bowel. *Nutrition* 1999;**15**:633–7.
4. **Goulet O.** Intestinal failure in children. *Transplant Proc* 1998;**30**:2523–5.
5. **Goulet O,** Ruemmele F. Causes and management of intestinal failure in children. *Gastroenterology* 2006;**130**(2 Suppl 1):S16–28.
6. **Vanderhoof JA,** Young RJ, Thompson JS. New and emerging therapies for short bowel syndrome in children. *Paediatr Drugs* 2003;**5**:525–31.
7. **Rudolph CD,** Hyman PE, Altschuler SM, *et al*. Diagnosis and treatment of chronic intestinal pseudo-obstruction in children: report of consensus workshop. *J Pediatr Gastroenterol Nutr* 1997;**24**:102–12.
8. **Goulet O,** Kedinger M, Brousse N, *et al*. Intractable diarrhea of infancy with epithelial and basement membrane abnormalities. *J Pediatr* 1995;**127**:212–9.
9. **Phillips AD,** Jenkins P, Raafat F, *et al*. Congenital microvillous atrophy: specific diagnostic features. *Arch Dis Child* 1985;**60**:135–40.
10. **Goulet OJ,** Revillon Y, Jan D, *et al*. Neonatal short bowel syndrome. *J Pediatr* 1991;**119**:18–23.
11. **Kelly DA.** Intestinal failure-associated liver disease: what do we know today? *Gastroenterology* 2006;**130**(2 Suppl 1):S70–7.
12. **Kocoshis SA,** Beath SV, Booth IW, *et al*. Intestinal failure and small bowel transplantation, including clinical nutrition: Working Group report of the second World Congress of Pediatric Gastroenterology, Hepatology, and Nutrition. *J Pediatr Gastroenterol Nutr* 2004;**39**(Suppl 2):S655–61.
13. **Agostoni C,** Axelson I, Colomb V, *et al*. The need for nutrition support teams in pediatric units: a commentary by the ESPGHAN committee on nutrition. *J Pediatr Gastroenterol Nutr* 2005;**41**:8–11.
14. **Goulet O,** Baglin-Gobet S, Talbotec C, *et al*. Outcome and long-term growth after extensive small bowel resection in the neonatal period: a survey of 87 children. *Eur J Pediatr Surg* 2005;**15**:95–101.
15. **Gupte GL,** Beath SV, Protheroe S, *et al*. Improved outcome of referrals for intestinal transplantation in the UK. *Arch Dis Child* 2007;**92**:147–52.
16. **Touloukian RJ,** Smith GJ. Normal intestinal length in preterm infants. *J Pediatr Surg* 1983;**18**:720–3.
17. **Beath S,** Pironi L, Gabe S, *et al*. Collaborative strategies to reduce mortality and morbidity in patients with chronic intestinal failure including those who are referred for small bowel transplantation. *Transplantation* 2008;**85**:1378–84.
18. **Annual BANS report**. Artificial nutrition support in the U.K. 2000–2005. 2005. http://www.bapen.org.uk/pdfs/bans_reports/bans_report_05.pdf (accessed Oct 2006)
19. **Vantini I,** Benini L, Bonfante F, *et al*. Survival rate and prognostic factors in patients with intestinal failure. *Dig Liver Dis* 2004;**36**:46–55.
20. **Koglmeier J,** Day C, Puntis JW. Clinical outcome in patients from a single region who were dependent on parenteral nutrition for 28 days or more. *Arch Dis Child* 2008;**93**:300–2.
21. **Kaufman SS,** Loseke CA, Lupo JV, *et al*. Influence of bacterial overgrowth and intestinal inflammation on duration of parenteral nutrition in children with short bowel syndrome. *J Pediatr* 1997;**131**:356–61.
22. **Andorsky DJ,** Lund DP, Lillehei CW, *et al*. Nutritional and other postoperative management of neonates with short bowel syndrome correlates with clinical outcomes. *J Pediatr* 2001;**139**:27–33.
23. **Torres C,** Sudan D, Vanderhoof J, *et al*. Role of an intestinal rehabilitation program in the treatment of advanced intestinal failure. *J Pediatr Gastroenterol Nutr* 2007;**45**:204–12.
24. **Diamond IR,** de Silva N, Pencharz PB, *et al*. Neonatal short bowel syndrome outcomes after the establishment of the first Canadian multidisciplinary intestinal rehabilitation program: preliminary experience. *J Pediatr Surg* 2007;**42**:806–11.
25. **Koletzko B,** Goulet O, Hunt J, *et al*. 1. Guidelines on paediatric parenteral nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), supported by the European Society of Paediatric Research (ESPR). *J Pediatr Gastroenterol Nutr* 2005;**41**(Suppl 2):S1–87.
26. **Jansen D.** The impact of a clinical nurse's role on CVC infections and bacteremia: a two year comparative, retrospective study. *Aust Nurs J* 1994;**1**:22–5.
27. **Bozzetti F,** Mariani L, Bertinet DB, *et al*. Central venous catheter complications in 447 patients on home parenteral nutrition: an analysis of over 100.000 catheter days. *Clin Nutr* 2002;**21**:475–85.
28. **Colomb V,** Fabeiro M, Dabbas M, *et al*. Central venous catheter-related infections in children on long-term home parenteral nutrition: incidence and risk factors. *Clin Nutr* 2000;**19**:355–9.
29. **Forbes A.** Achieving and maintaining venous access for home parenteral nutrition. *Curr Opin Clin Nutr Metab Care* 2005;**8**:285–9.
30. **Bucuvalas JC,** Goodrich AL, Blitzer BL, *et al*. Amino acids are potent inhibitors of bile acid uptake by liver plasma membrane vesicles isolated from suckling rats. *Pediatr Res* 1985;**19**:1298–304.
31. **Gura KM,** Duggan CP, Collier SB, *et al*. Reversal of parenteral nutrition-associated liver disease in two infants with short bowel syndrome using parenteral fish oil: implications for future management. *Pediatrics* 2006;**118**:e197–201.
32. **Kaufman SS.** Prevention of parenteral nutrition-associated liver disease in children. *Pediatr Transplant* 2002;**6**:37–42.
33. **Messing B,** Zarka Y, Lemann M, *et al*. Chronic cholestasis associated with long-term parenteral nutrition. *Transplant Proc* 1994;**26**:1438–9.
34. **Colomb V,** Dabbas-Tyan M, Taupin P, *et al*. Long-term outcome of children receiving home parenteral nutrition: a 20-year single-center experience in 302 patients. *J Pediatr Gastroenterol Nutr* 2007;**44**:347–53.
35. **Sondheimer JM,** Asturias E, Cadnapaphornchai M. Infection and cholestasis in neonates with intestinal resection and long-term parenteral nutrition. *J Pediatr Gastroenterol Nutr* 1998;**27**:131–7.
36. **Salvia G,** Guarino A, Terrin G, *et al*. Neonatal onset intestinal failure: an Italian Multicenter Study. *J Pediatr* 2008;**153**:674–6, 676.
37. **Colomb V.** Economic aspects of paediatric home parenteral nutrition. *Curr Opin Clin Nutr Metab Care* 2000;**3**:237–9.
38. **Longworth L,** Young T, Beath SV, *et al*. An economic evaluation of pediatric small bowel transplantation in the United Kingdom. *Transplantation* 2006;**82**:508–15.