Nutritional care and candidates for small bowel transplantation

S V Beath, I W Booth, M S Murphy, J A C Buckels, A D Mayer, P J McKiernan, D A Kelly

Abstract

Twenty two children were evaluated for small bowel transplantation between 1989 and 1994. Eight were unfit for transplantation and died within three months; a raised plasma bilirubin concentration ($>200 \mu\text{mol/l}$) predicted death from liver failure within six months ($p=0.0001$). The 11 children who were not managed by a multidisciplinary nutritional care team were less well nourished at referral, had more complications with intravenous feeding catheters, and greater early mortality while awaiting transplantation ($p<0.05$). It is recommended that children with chronic intestinal failure be referred for assessment early, before liver dysfunction is established.

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Parenteral nutrition permits children with chronic intestinal failure, who would otherwise have died in infancy, to survive for many years. It is associated with a number of life threatening complications such as line sepsis, hepatic dysfunction, loss of venous access,^{1,2} and pulmonary embolism.³ Even children on long term parenteral nutrition managed at home experience a range of psychosocial and physical problems requiring constant vigilance and support.⁴

Intestinal transplantation is a logical extension of treatment for patients with complications related to parenteral nutrition, but transplant programs have been restricted by the uniquely intense rejection that occurs in the small bowel.⁵ Isolated intestinal transplants and combined liver and bowel transplants have been undertaken since the 1960s,^{6–8} but results did not improve until tacrolimus (FK506) became available. Tacrolimus is a similar but more potent immunosuppressant than cyclosporin and has been associated with results improving to 65% overall survival in 32 paediatric recipients over four years in Pittsburgh⁹ with approximately 50% survival in 100 operations reported world wide.¹⁰ The choice of isolated intestinal transplantation or combined with liver, depends on the extent of hepatic damage at the time of transplantation. The observation that concomitantly transplanted liver enhances tolerance to kidney and other organ allografts from the same donor,¹¹ and that many patients are referred late, has caused combined small bowel and liver

transplantation to be adopted as the operation of choice in developing transplant programs. However, initial results of isolated intestinal transplantation (70–90% one year survival) compare favourably with the combined operation.^{9,12,13} The role of the liver in enhancing survival of other grafts may be offset in the case of small bowel transplantation by the effect of escalating hepatic dysfunction in patients who are referred late.

These initial results have stimulated considerable interest and increased referrals of children on long term parenteral nutrition for assessment for isolated or combined transplantation. As many children on long term parenteral nutrition have a satisfactory quality of life,¹⁴ it is important to establish the appropriate point at which patients should be referred for assessment. Late referral may have serious consequences because patients often experience a long delay before suitable donor organs become available.¹⁵ We have evaluated our experience of 22 patients referred for small bowel and/or liver transplantation.

Patients and methods

Between September 1989 and September 1994, 22 children (age range 4 months–13 years) with chronic intestinal failure secondary to short gut ($n=12$), pseudo-obstruction ($n=7$), and enteropathy ($n=3$) were evaluated for small bowel transplantation. Nutritional status was assessed by measuring weight, height, mid-arm circumference, and triceps skinfold thickness. The duration of parenteral nutrition, number of feeding catheters, frequency of line sepsis, patency of central veins, hepatic function, and histology at the time of referral were recorded.

Results

The duration of parenteral nutrition ranged from four months to six years. Twelve children had overt liver disease (bilirubin 120–760 $\mu\text{mol/l}$) and 10 had severe problems with venous access. All had splenomegaly, eight children had oesophageal varices and ascites, and 17 had abnormal histology on liver biopsy (13 cirrhosis, four fibrosis). All the children were followed up for three to 14 months. Twelve died without undergoing transplantation: eight were too ill to place on the transplant list and four died while awaiting a donor. Except for two children (one died of multiple pulmonary emboli, the other died of sepsis), all the deaths were secondary to liver failure. Two children have undergone combined small bowel and liver transplantation. One died from

Institute of Child Health, University of Birmingham

S V Beath
I W Booth
M S Murphy

Queen Elizabeth Hospital, Birmingham
J A C Buckels
A D Mayer

The Liver Unit, The Children's Hospital, Birmingham
P J McKiernan
D A Kelly

Correspondence to:
Dr S V Beath, The Liver Unit, The Children's Hospital, Ladywood Middleway, Birmingham B16 8ET.

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Relationship between plasma bilirubin concentration at evaluation for small bowel and liver transplantation and duration of survival before death from liver failure ($n=19$); three subjects who died of infection not included. There was a tenfold relative risk of dying if bilirubin concentration was $>200 \mu\text{mol/l}$ by Fisher's exact test.

infection six months after the procedure and one died from pulmonary haemorrhage after six weeks. Seven children remain under observation and are not considered to require transplantation at present. One child is awaiting transplantation.

In those children who died of liver failure, plasma bilirubin concentration at the time of evaluation was related to duration of survival (figure). The relative risk of dying of liver failure within six months was tenfold higher in children with a plasma bilirubin greater than $200 \mu\text{mol/l}$ at the time of assessment compared with those below $200 \mu\text{mol/l}$ ($p=0.0001$, Fisher's exact test). We noted a marked discrepancy in clinical status between children referred for evaluation from centres with and without nutritional care teams and therefore compared these two groups in more detail.

Eleven children had been managed in a centre with an established nutritional care team comprising a nurse specialist, a dietitian, a pharmacist, a social worker, and a clinician. At referral, nutritional status was better ($p=0.05$) and venous catheter survival longer ($p=0.03$) in those children managed in centres with a nutritional care team compared with those without (see table). Short term mortality (death within three months of evaluation) was

much higher ($p=0.03$) in the children referred from centres without a nutritional care team.

Discussion

These data suggest that the development of liver disease adversely affects survival in this group of patients particularly in the context of the shortage of donors suitable for young children.^{9 15} The children from centres with multidisciplinary care teams were significantly better nourished and had experienced fewer central venous line changes than the children managed in centres without a nutritional care team. These observations are consistent with previous findings from this centre supporting the value of a multidisciplinary approach to the management of these children.^{16 17}

The occurrence of parenteral nutrition related liver disease is more common in children, especially premature neonates requiring emergency abdominal surgery.^{1 2} This may be related to the relatively high nutritional requirements for parenteral nutrition infusions in infancy, hepatic immaturity in disposing of potentially toxic substances, for example manganese, and recurrent sepsis either from the intravenous feeding catheter or from bacterial overgrowth in the bowel.^{18 19} Avoidance of complications depends on a multidisciplinary team that can minimise line blockages and infections,¹⁶ monitor the composition of parenteral nutrition solutions and plasma biochemistry including trace elements and liver function tests.¹⁷ Nutritional care teams can ensure that residual gut function is maximally utilised with special feeds, tube feeding, and treatments such as antibiotics for bacterial overgrowth and motility agents (for example cisapride,²⁰ erythromycin,²¹ loperamide).

Despite optimal management, some children develop liver disease and will need combined small bowel and liver transplantation. Potential candidates for small bowel transplantation should be referred for assessment early, either when splenomegaly develops or when the conjugated bilirubin concentration goes above $100 \mu\text{mol/l}$. As experience with intestinal transplantation grows, it may be possible to offer transplantation to patients who are stable on home parenteral nutrition before hepatic dysfunction develops. Currently, limited organ availability and postoperative problems with immunosuppression^{9 10 22 23} dictate that small bowel transplantation is reserved for those who are likely to die from complications of parenteral nutrition within one year.

Thus, nutritional care teams provide an essential service for children with intestinal failure who are awaiting small bowel transplantation because they contribute to their longer survival and greater size, which gives them an advantage in the search for suitable donor organs.

The assessment and management of these children was facilitated by members of the dietetic and pharmacy departments, and nursing colleagues in particular Chris Holden, Patrick Ball, and Gill Brook. The skilful replacement of feeding catheters was undertaken by colleagues in the departments of surgery and cardiology at The Children's Hospital.

Clinical features at the time of referral and outcome in children managed in centres with and without nutritional care teams; values are median (range) except where otherwise stated

	Centre with nutritional care (n=11)	No nutritional care (n=11)	p Value*
Weight z score	-0.5 (-2.1 to 0.82)	-1.8 (-5.8 to 0.39)	0.05
Height z score	-1.7 (-3.1 to -0.3)	-2.6 (-5.7 to -0.2)	0.2
Interval between line changes (months)	5.5 (0.8-12)	2.1 (1.3-3)	0.03
Age (months)	29 (4-159)	11 (6-34)	0.2
Bilirubin ($\mu\text{mol/l}$)	20 (12-581)	240 (10-760)	0.3
No (%) of patients dying within three months	1 (17)	7 (87.5)	0.03

*By Mann-Whitney except for number of patients dying within three months (Fisher's exact test).

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