

Home parenteral nutrition in adults : the current use of an experienced method

A. Van Gossum¹, I. Peeters², V. Lievin³

Medico-surgical Department of Gastroenterology (1), Nurse in charge of HPN program (2), Department of Pharmacy (3) ; Nutrition Team, Hôpital Erasme, ULB, Brussels.

Abstract

Home parenteral nutrition (HPN) is now commonly used in industrialized countries. In Europe, the mean incidence of newly enrolled cases is about 3 patients per 10⁶ inhabitants, per year. The use of HPN is much larger in North America.

Cancer has become the largest single indication of HPN over the world. The complications are either related to the central catheter (sepsis, thrombosis, migration) or metabolic (liver abnormalities, bone disorder, deficiencies).

Complications rate may be lowered by an adequate nutritional regimen, a good teaching of the patients and the presence of a nutritional team in specialized centres.

The survival probability for patients with benign diseases is about 65% at 5 years. The mortality rate related to HPN itself is less than 10%.

For patients with benign diseases, weaning of HPN is observed in 40 to 70% of the cases. Sixty percent of the patients have a very good quality of life.

HPN must be used selectively in cancer patients. (*Acta gastroenterol. belg.*, 1999, 62, 201-209).

Epidemiology

The use of parenteral nutrition administration started in the early sixties. Schils *et al.* tried to maintain a patient at home on parenteral nutrition (HPN) (1). Although this patient only survived during a few months, several teams, in North America and in Europe, initiated a program of HPN during the seventies. Subsequently, many groups reported their initial experience with HPN, mentioning a low incidence of complications and a good survival rate (2-4).

According to the data collected by the North America Registry on HPN patients, the estimated number of HPN patients in the US was approximately 18,000 in 1986 and reached 40,000 in 1992 (5,6). A multicenter survey performed in 12 European countries in 1993 showed a mean incidence and prevalence of 2-3 newly enrolled patients on HPN per 10⁶ inhabitants (7). The increased use of HPN in Europe is obvious when comparing data obtained in 1986 and in 1993 and also according to the results of a prospective survey that was performed in France from 1993 to 1995 (7-9).

However, use of HPN is still ten times higher in the US than in Europe. HPN is routinely used in Japan (10), Israel (11) and Australia (12). In the European survey, age distribution of the patients at the onset of HPN was as follow : 36% (from 16 y. to 40 y.), 41% (from 41 y. to 60 y.), 14% (from 61 to 70%) and 9% (over 70 y.) (7).

Indications

Overall, the distribution of underlying diseases requiring HPN is quite similar in Europe, the US and Japan (6,7,10). Cancer has become the largest single indication of HPN over the world (40%). Crohn's disease, mesenteric vascular diseases, radiation enteritis and disorders of intestinal motility remain the most frequent benign conditions requiring long-term HPN. HPN is also used in AIDS patients with intractable diarrhea. However, the number of AIDS patients receiving HPN recently decreased since the introduction of more efficacious tritherapy. We have to underline that 25% of HPN patients are suffering of "miscellaneous" diseases, including chronic pancreatitis, intestinal mucosa atrophy, anorexia nervosa, cachexia, etc...

However, the distribution of underlying diseases in HPN patients varies among the different European countries (7). Crohn's disease accounts for 50% of indications in UK but only for 2% in Italy ; on the contrary, cancer represents 67% of indications in Italy and 8% in UK. If we consider the benign diseases, the most common indications are small bowel resection, digestive fistulas and motility disorders. For cancer patients, the main indication is intestinal obstruction which is common in case of peritoneal carcinomatosis. Intractable diarrhea associated with severe malnutrition is the major indication in AIDS patients (6,7).

Perfusion regimen

Perfusion of nutritional solutions is performed on a cyclical nocturnal basis in the majority of the patients. The regimen allows more autonomy during the daytime for HPN patients (13). Contra-indications for the cyclical regimen are cardiac or renal failure or the need to infuse large volumes of solutions (more than 3.5 liters/day). Cyclical regimen has several metabolic advantages : an increased rate of lipid oxidation, a decrease of lipid storages, an increase in lean mass and visceral proteins (14,15). In adults receiving cyclical nocturnal HPN, volumes of 1.5 to 3.5 liters may be administered in a 10 to 16 hour period. Nocturnal

Address for correspondence : André Van Gossum, Department of Hepato-Gastroenterology and Pancreatology, Erasme Hospital, Free University of Brussels, Route de Lennik, 808, B-1070 Brussels, Belgium.

diuresis is the only discomfort of cyclical perfusion in many patients.

Nutritional solutions may be packed in separate bottles or in all-in-one bags (16). The use of all-in-one bags decreases the number of manipulations and therefore, the duration of teaching as well as the risk of catheter infection. The risk of vein thrombosis seems also to be lower when using the all-in-one regimen. Moreover, delivery and storage of all-in-one bags are facilitated. Disadvantages of the all-in-one system are related to a moderately increased risk of catheter thrombosis and to an decreased stability of vitamins (17). To avoid this problem, it is recommended to rinse the intravenous line with 100 ml of saline solutions before injecting heparin, at the end of the perfusion. Moreover, protection of all-in-one bags against day light may lower the risk of vitamins degradation in the mixture solution (18).

Pump regulation of the flow lowers the risk of catheter obstruction (200 to 300 ml/hour) as well as the risk of hypoglycemia because of a progressive tapering of the flow (19).

In the majority of the cases, administration of nutritional solutions is performed through a subcutaneous tunnelized catheter and is positioned in the vena cava via the internal jugular vein or a subclavian vein, preferentially on the right side (20). Based on the reports of the North America Registry on HPN and the European surveys, the use of subcutaneous reservoirs (port-a-cath) is growing (6,7). This trend is due, on one hand, to its wide use in cancer patients who receive chemotherapy and, on the other hand, to the willingness of some patients who prefer implantable catheters for functional and esthetic reasons, for instance for practicing aquatic sports or for taking a shower (7,21).

The number of perfusions that are administered per week may vary along in time in function of intestinal adaptation capacities. The European survey has shown that the percentage of bags/week was as follows : 7 (67%), 6 (9%), 5 (12%), 4 (8%), or less (4%) (7).

Oral feeding is not only allowed but also encouraged in patients without bowel obstruction or need for bowel rest (22). It has been shown that patients with short bowel are in fact hyperphagic (23). In the 1993 European survey, 37% of patients had free oral intakes, 27% had limited oral intakes, while 33% ingested nothing (7).

An enteral feeding is sometimes combined with HPN. The amounts of proteins and calories are adapted in function of the requirements and the residual intestinal capacity. For many HPN patients, parenteral support may mainly compensate water and electrolyte losses. That is crucial in presence of very short bowel or high output jejunostomy. HPN patients require complementary support in vitamins and in trace elements. Among them, zinc and selenium are the most important, especially in case of large output of intestinal fluids (24). In case of long-term administration of lipid emulsions, supplementation in vitamin E is mandatory

because of the low content in vitamin E of the lipid emulsions that are very rich in W_6 fatty acids (TCL). Indeed, prolonged administration of lipid emulsions may induce vitamin E deficiency and increase the level of lipid peroxidation (25). For patients with high output jejunostomy (more than 3 liters/day) subcutaneous administration of octreotide may lower the digestive losses (26).

Complications

Catheter-related sepsis

Catheter sepsis constitutes the most frequent as well as the most harmful complication of Home Parenteral Nutrition (HPN) management. Indeed, catheter infection represents 50% of the causes of death that are directly related to HPN (13). The real incidence of catheter infection remains unknown due to the difference in criteria of catheter sepsis that have been used in the literature (8,33-38). However, on basis of several series, catheter infection in HPN patients has been estimated at 0.34 episodes per patient per year. The onset of fever — with or without chills — that occurs during the administration of parenteral nutrition is the classical manifestation of catheter infection. Nevertheless, catheter sepsis may occur in some cases with mild subclinical pyrexia or hypotension without fever (33, 39,40).

Catheter infection may be due to bacterial contamination of parenteral solutions, to catheter infection during handling, to infection of the exit site of the catheter or to bacterial contamination of the line during a septicemia originating from another site. Infections of the subcutaneous exit site of the catheter account for 5 to 43% of the cases of catheter sepsis (5,29,41). Episodes of catheter infection in HPN patients are mainly related to gram-positive bacteria (such as *Staphylococcus epidermidis*; 45-70%), then, to gram-negative ones, and, less frequently, to fungal species (*Candida*: 3-15%) (33,43). In 10 to 15% of the cases, infection is polymicrobial (33). When catheter-sepsis is suspected, it is mandatory to rapidly perform blood culture from a peripheral vein and via the central line, simultaneously (43,44). The central line is considered to be the source of infection when the number of bacterial colonies is four times higher in the catheter than in the peripheral blood, or when the number of colonies is superior to 100 CFU/ml in the blood that has been collected with the central line. Some methods allow to detect catheter sepsis more rapidly (45,46). In case of cutaneous reddening or purulent discharge around the exit site of the catheter, culture of the skin as well as the hub and exit site must be performed. Catheter infection is confirmed in culturing the tip of the catheter by semi-quantitative or quantitative methods (48,49).

The presence of a central vein thrombosis appears to be a risk factor for the occurrence of catheter

sepsis (50). In a recent study, a vein thrombosis was observed in 20% of the catheter infection. O'Keefe *et al.* have reported a series of 41 patients of which seven presented recurrent episodes of catheter sepsis (42). In 5 out of 7 of them, a venous thrombosis was present. According to their experience, these authors suggested that patients who are at risk for developing recurrent catheter sepsis had the following characteristics : young age, Crohn's disease, jejunostomy, smoker and poor technique of catheter manipulation. Although Raviglione *et al.* (51) reported a higher incidence of catheter-related sepsis in HPN patients with AIDS, it was not confirmed by other teams (52,53). There is no evidence that an external catheter is more likely to get infected than a subcutaneous implanted reservoir (54). Nevertheless, it appears more difficult to sterilize an implanted reservoir than an external catheter in case of sepsis.

When an infectious is suspected, a systematic removal of the catheter must be avoided. Indeed, a prospective study has shown that 70% of the catheters that were removed were in fact not infected (55,56). An immediate withdrawal of the catheter is mandatory in presence of a septic shock with hemodynamic alterations. The removing of the catheter seems also indicated in presence of visible signs of infection of the subcutaneous tunnel or in presence of bacteria such as *Staphylococcus aureus* and *Pseudomonas*. While some teams claimed successful treatment of catheter infected with these latter bacteria, removing the line seems more appropriate in these conditions (48,57,58). Before receiving the results of bacterial investigations, a large-spectrum antibiotic that covers gram-positive and gram-negative bacteria should be administered (Vancomycin 1-2 mg/kg or Amikacin 1.5 to 3 mg/kg); the antibiotics are subsequently adapted to the profile of the bacteria. Antibiotics may be infused via a peripheral vein or via the infected central catheter.

Administration can be continuous or intermittent in using the antibiotic-lock system that has been described by B. Messing *et al.* (59). A control of the sepsis could be achieved in 90% of the cases with a risk of recurrent sepsis lower than 5%. This procedure allows to reduce the duration of the hospitalization and to provide the treatment ambulatory at home. It seems recommended to discontinue the administration of nutritional support up to the disappearance of fever. Duration of antibiotic administration is not well defined but should last at least 2 weeks.

Some teams have recommended the simultaneous administration of streptokinase or urokinase in relation to the high incidence of concomitant venous thrombosis.

Venous thrombosis

The mean incidence of central venous thrombosis (CVT) is 0.027 episodes per catheter per year (8, 27,32,38,61,62). Clinical manifestations of CVT are chest pain, radiating to the shoulders and the neck (62). The appearance of edema in the collateral arm is

sometimes described. In some cases, fever may be present with or without catheter infection. Formation of venous thrombosis is due to adsorption of proteins and fibrinogen at the surface of the catheter that favors platelets aggregation and coagulation products activation (63).

Central venous thrombosis is facilitated by exogenous and endogenous factors : coagulopathy, inflammatory bowel diseases, location of the tip of the catheter in the vena cava superior, type of the catheter (PVC > silicone > polyurethane) and type of nutritional solutions (glucose > aminoacids > lipids) (64,65,66,67). Prevention of CVT implies the choice of the catheter, the right positioning of the catheter and the restriction of hypertonic glucose solutions. Some studies have shown the protective effect of administrating small doses of warfarin (68,69,70).

Some groups advocate to administer therapeutic doses of warfarin in patients who have developed CVT on prophylactic regimen (68). However, prophylactic administration of anticoagulation failed to decrease the incidence of CVT in AIDS patients (71). Thrombolysis by injecting intravenous streptokinase seems to be efficacious in the majority of cases of CVT (73,73). The withdrawal of the catheter combined with heparin or coumarine administration do not allow to restore the vacuity of the central vein. It has been reported that the placement of expandable vascular stent into the thrombotic vein may restore the blood flow with or without thrombolysis (74).

Occlusion

The mean incidence of catheter occlusion is about 0.077 episode per catheter per year (8,27,31,32,37,52,62). That may be due to precipitation of calcium phosphate or to blood reflux with blood clogging inside the lumen of the catheter. Injection of streptokinase may restore the flow in the majority of the cases (75). In case of intermittent blockade, one may suspect deposition of phospholipids that could induce precipitation of trace elements or minerals. That could be prevented by separate infusion of lipids or systematic rinsage of the catheter at the end of the perfusion period (76).

Migration

Catheter migration is a rare event (0.05 to 0.1 episode per catheter per year) and may be prevented by a subcutaneous tunnelization of the catheter and the fixation of the catheter with a sacron ring (6,8,27,78).

Liver complications

Liver abnormalities

Liver abnormalities related to long-term parenteral nutrition (PN) range from mild liver enzyme elevations to cirrhosis. Despite 30 years of experience, the cause,

pathogenesis and treatment of PN-related hepatic and biliary dysfunction are not perfectly understood. Three distinctive clinical syndromes dominate: steatosis and steatohepatitis which predominate in adults, cholestasis syndrome that is more frequent in young patients, and biliary sludge formation and cholestasis which are common for both groups (79).

Incidence

The actual incidence of liver abnormalities is not well defined. Indeed, with a better understanding and more adequate use of PN, metabolic complications have become less frequent. The incidence of abnormal hepatic enzyme levels has been variably reported from 25 to 100% (79,80). In a recent European survey, in which 53 centres were included, liver histological ranged from 0-40% for fatty liver to 0-25% for cirrhosis. In 1988, 4.6% of hospital readmission in patients on home PN in USA were for organ dysfunction (6).

So, severe hepatic problems are rare but minor abnormalities are probably very common. To some extent the incidence of abnormalities will vary according to how thoroughly the patient is investigated.

Etiopathogenicity

Factors that have been implicated in the pathogenesis of PN-induced liver injury are either related to the parenteral nutrition itself or patient-dependent. Nutrition-dependent factors include hypercaloric PN infusion, inadequate or excess of lipid, aminoacid excess, antioxidant deficiency, duration of PN, etc. This section is mainly focused on patient-dependent factors.

Steatosis

Hepatic fat accumulation was formerly a common occurrence during total parenteral nutrition in adults. Clinically, steatosis is rarely symptomatic but may cause right upper quadrant discomfort and hepatic tenderness (81).

Mild increase of transaminases, accompanied less frequently by elevated alkaline phosphatase and bilirubin levels, are the biochemical features of steatosis. Enzymatic perturbations usually occur within 2 weeks after initiating PN and can usually be expected to return to normal despite maintenance of the same regimen. Steatosis is well detected by liver ultrasonography examination.

Whereas steatosis seems to be directly related to the delivery of an inappropriate carbohydrate load, general conditions of the patient may aggravate fat deposition in the liver: starvation, protein-caloric malnutrition or glucose intolerance (82-85).

PN-induced steatosis in adults may be the result of decreased fatty acid oxidation or mobilization, increased fatty acid synthesis or increased influx of fatty acids with entrapment in the liver, or decreased lipoprotein synthesis or secretion.

In normal conditions, the triacylglycerol released into the blood will be hydrolyzed in the adipose tissue by lipoprotein lipase and the fatty acids will be taken up by that tissue, esterified, and stored without being released into the general circulation. In starvation, the activity of lipoprotein lipase in adipose tissue decreases; the triacylglycerol in the blood is, therefore, directed to other tissues (86).

Cholestasis

Intrahepatic cholestasis may develop as soon as 5 days after initiation of TPN but generally occurs somewhat later than steatosis, approximately 20 days after the start of PN. It is initially associated with mild to moderate elevations in serum alkaline phosphatase and may be followed by elevated bilirubin levels (87).

The role of patient-dependent factors seems more important in the pathogenesis of cholestatic syndrome than in steatosis.

Lack of oral intake, through its effect on bile flow and secretion, may be a major factor in PN-related complications. That could also impair the integrity of the intestinal barrier and promote translocation of bacteria across the gut wall. Bacterial translocation could be source of sepsis or release of endotoxins that could increase cytokines (such as TNF- α) production (88).

Obviously, preexisting hepatic dysfunction may facilitate cholestasis or increase susceptibility to sepsis. The coexistence of an uncontrolled sepsis can also contribute to liver enzyme abnormalities or even to "septic jaundice".

The hyperbilirubinemia that may develop in patients on long-term PN has been also associated with medications, hemolysis, anesthetics, hematoma and tissue trauma and is often difficult to distinguish from a PN effect alone.

It has been also reported that the incidence of liver enzyme abnormalities during PN is increased in patients with inflammatory bowel diseases and malignancies.

It has been well shown that anatomical modifications may also increase the risk of developing cholestasis on long-term PN: a very short-bowel (< 150 cm), an ileopathy or ileal resection, a resected or remaining excluded colon. These anatomical factors could play a role through the alteration of bile salt composition. Perturbations of the enterohepatic circulation of bile salts may contribute to liver injury. Intestinal stasis along with bacterial overgrowth in the small intestine promotes intraluminal bile salt deconjugation and leads to an increased production of lithocholic acid (by 7 α -dehydroxylation of chenodeoxycholic acid), that has been shown to impair bile flow.

In patients with very short bowel, loss of some endogenous nutrients or protective factors such as antioxidant could potentially play a role (89-93).

It has been also suggested that hypoxic situations may favor the development of cholestasis. In premature

infants, pool size, synthesis and intestinal concentration of bile are lower than in full term infants, suggesting a relative immaturity of the biliary secretory system.

Disorders of the gallbladder and biliary tract

Acalculous cholecystitis, biliary sludge, gallbladder distension, and gallstones have been reported in association with PN in both children and adults. As it was expected, disease or resection of the distal ileum promotes gallstone development in these patients, inducing alteration of bile composition and lowering bile salt pool (94).

It also appears that absence of oral intake has deleterious effect on biliary function by inducing a loss of enteric stimuli, an impaired gallbladder emptying and bile flow (95).

Recommendations to limit patient-dependent factors of PN-related liver dysfunction

Although it is not possible to interact with all the patient-dependent factors that are likely to induce liver abnormalities, following guidelines are recommended :

- 1 To initiate as soon as possible some oral intake of food or small amounts of enteral nutrition.
- 2 To limit bacterial overgrowth by resecting intestinal strictures or remnant excluded intestine or by giving antibiotics such as metronidazole.
- 3 To protect bile salt composition by providing ursodeoxycholic acid.
- 4 To discontinue (if possible) PN in patients with biopsy-proven cirrhosis or progressively worsening intrahepatic cholestasis. Intestinal transplantation is becoming a potential alternative.
- 5 To propose a prophylactic cholecystectomy in high-risk patients.

Bone complications

In the early months of treatment, HPN is associated with hypercalciuria and accelerated bone turnover. Thereafter, an adaptative response develops to lower the extent of calciuria, with a shift toward normal or positive bone turnover, but not in all the patients (96). The skeletal pathology observed in long-term HPN is heterogeneous, characterized by osteopenia, with low or normal bone formation per tissue volume (bone formation rate- and, occasionally, hyperosteoridosis (97,98).

Several groups have shown that the majority of HPN patients had a decreased mineral bone content at the start of HPN because of chronic malabsorption, prolonged immobilization or chronic usage of steroids (99).

De Vernejoul *et al.* described a low remodeling bone disease characterized by lower than normal mean trabecular bone volume, a uniform absence of increased osteoid, and a marked reduction of bone formation with subnormal osteoclastic activity (100). Presence of aluminum stains, excessive load of aminoacids and

hypersensitivity to vitamin D have been suggested as predisposing factors to bone disease (101,102).

Rare longitudinal studies performed in long-term HPN patients have shown heterogeneous outcome of bone mineral content (103-106). Verhage *et al.* conducted a prospective study on the effect of long-term withdrawal of vitamin D in HPN patients (107). They reported an improvement of bone mineral content (18%) after discontinuing vitamin D administration in long-term HPN. Calcium, phosphorus, magnesium and 25 vitamin D remained normal. Parathormone and 1.25 vitamin D levels — that were initially low — became normal. These authors recommended that patients with metabolic bone disease should have their levels of PTH, 1.25 OH vit. D and 25 OH vit. D levels regularly measured. When PTH and 1.25 OH vit. D levels are low, and 25 OH vit. D levels normal, then vitamin D should be withdrawn from HPN solution.

A recent European survey showed that strategy in face of bone abnormalities in HPN patients is still controversial and heterogeneous (108).

Miscellaneous complications

Several biochemical and clinical alterations have been reported in HPN patients. Most of the metabolic complications were related to trace elements or vitamins deficiencies. Routine administration of vitamins and trace elements mixtures is mandatory to prevent deficiencies. Supplementary supply in zinc and selenium are necessary in case of high amount of digestive losses for preventing acrodermatitis, muscular weakness or even cardiomyopathy (109,110). Glucose intolerance associated with neuropathy — sometimes mimicking metronidazole side-effects — has been described in presence of chromium deficiency (111,112). Neurological alterations with extrapyramidal manifestations that have been observed in HPN patients have been attributed to manganese deposits in the brain. IMR-T1 signal in basal ganglia is the best way for detecting accumulation of manganese in the brain (114).

Combined administration of heparin and subcutaneous octreotide in a patient on HPN may provoke hyperkaliemia despite low intake of kalium (115). We underline that intakes in copper and manganese must be limited in presence of cholestasis (24).

Prognosis

Several studies have shown that survival is linked to the underlying disease. In a European survey performed in 1994, mortality rate after a 6 to 12 month follow-up period was zero in Crohn's disease, 7% in radiation enteritis, 8% in vascular diseases, 13% in miscellaneous but 71% in cancer and 88% in AIDS (7). The North America HPN Registry reported similar results (6). B. Messing *et al.* performed a study on 217 HPN patients with benign diseases and that have been enrolled in a HPN program between 1980 and 1989

in Belgian — French specialized centres (116). Seventy three patients died during the follow-up period. Mortality rate due to HPN was 11%. This work showed a survival probability at 1, 3 and 5 years of 91%, 70% and 62%, respectively. Multifactorial analysis of prognostic factors showed that independent factors associated with a good survival rate were: a age below 40 y. at the start of HPN, initiation of HPN after 1987 — that was reflecting the experience of the center — and the absence of chronic intestinal obstruction.

So, for patients who were less than 60 y., with a small bowel and having started HPN in 1987, the 2-year survival rate was estimated at 90%.

In this study — Crohn's disease — that was suggested to be a good prognostic factor — was not a independent parameter in the multivariate analysis. Amongst HPN patients with benign diseases, the cause of mortality was the underlying disease (30%), HPN itself (10%) or, independent (51%) or unknown (8%).

Several series confirmed that the mortality rate related to HPN itself is less than 10% (6,27). More than half of the cancer patients died within a 6-month period after starting HPN.

Patients with gynecologic cancer have a low survival duration (28,117). However, it seems that a subgroup of cancer patients (20%) may survive more than one year (6,7,118).

Weaning

Reasons for discontinuing HPN are intestinal adaptation, inability of the patient to cope with HPN or death. Rehabilitation rate is depending of the underlying disease, indication of HPN or duration of follow-up. In cancer patients, HPN is discontinued in 60% to 100% due to the patient's death (6,7). In some series, weaning is possible in 10 to 20% of cancer patients in a 6-to 12 month follow-up period (115,119). For patients with benign diseases, weaning of HPN is observed in 40 to 70% of the cases (6,27). In case of Crohn's disease, we must consider separately patients requiring short-time HPN in case of recurrence of a post-surgical short bowel syndrome.

Intestinal adaptation occurs mainly within the first 3 months of HPN but can be extended up to 2 years. After a 24 year period, HPN dependence is probably definitive. Byrne T. *et al.* have recently shown that simultaneous administration of growth hormones, glutamine and fiber-enriched diet may improve adaptation of the residual bowel (120). In a group of 15 patients with short bowel, 40% of patients were likely to be weaned off HPN and 40% could decrease their parenteral support. However, this study has not yet been confirmed.

Rehospitalization

Frequency and duration of rehospitalization are function of the severity of the underlying diseases and

the quality of patients' teaching. Several teams reported a rate of rehospitalization ranging from 1 to 2 episodes per year (6). In other teams, median duration of rehospitalization estimated as a percentage of HPN duration is approximately 10%, due partly to the underlying disease and partly to HPN complications (8,119). Catheter infection is the major cause of HPN related complication.

Quality of life

One of the major goals of HPN is to improve the quality of life of the patients allowing social, familial and professional rehabilitation. Cyclic nocturnal HPN allows a diurnal autonomy. In a multicenter study, Messing *et al.* showed that rehabilitation was better for patients less than 65 y. and for patients with Crohn's disease (8). Several teams estimate that 60% of their HPN patients have an acceptable quality of life. Less than 10% of patients require complete assistance at home (13,27,30,32,121,122).

Richards *et al.* described the lowest scores of quality of life in elderly patients or in narcotic-dependent patients (123). Although quality of life is important, it is systematically assessed in only 20% of HPN programs (71). Moreover, some particular aspects of the quality of life (for instance: travelling capacity, sexual activity...) are not always considered. In cancer or AIDS patients, quality of life has not been reported (28,124).

In conclusion, long-term parenteral nutrition is a safe method for providing nutrients in patient with transient or definitive intestinal failure. Complications rate can be lowered by administering adequate nutrition, and a good teaching and follow-up of the patient performed by a specialized nutrition team.

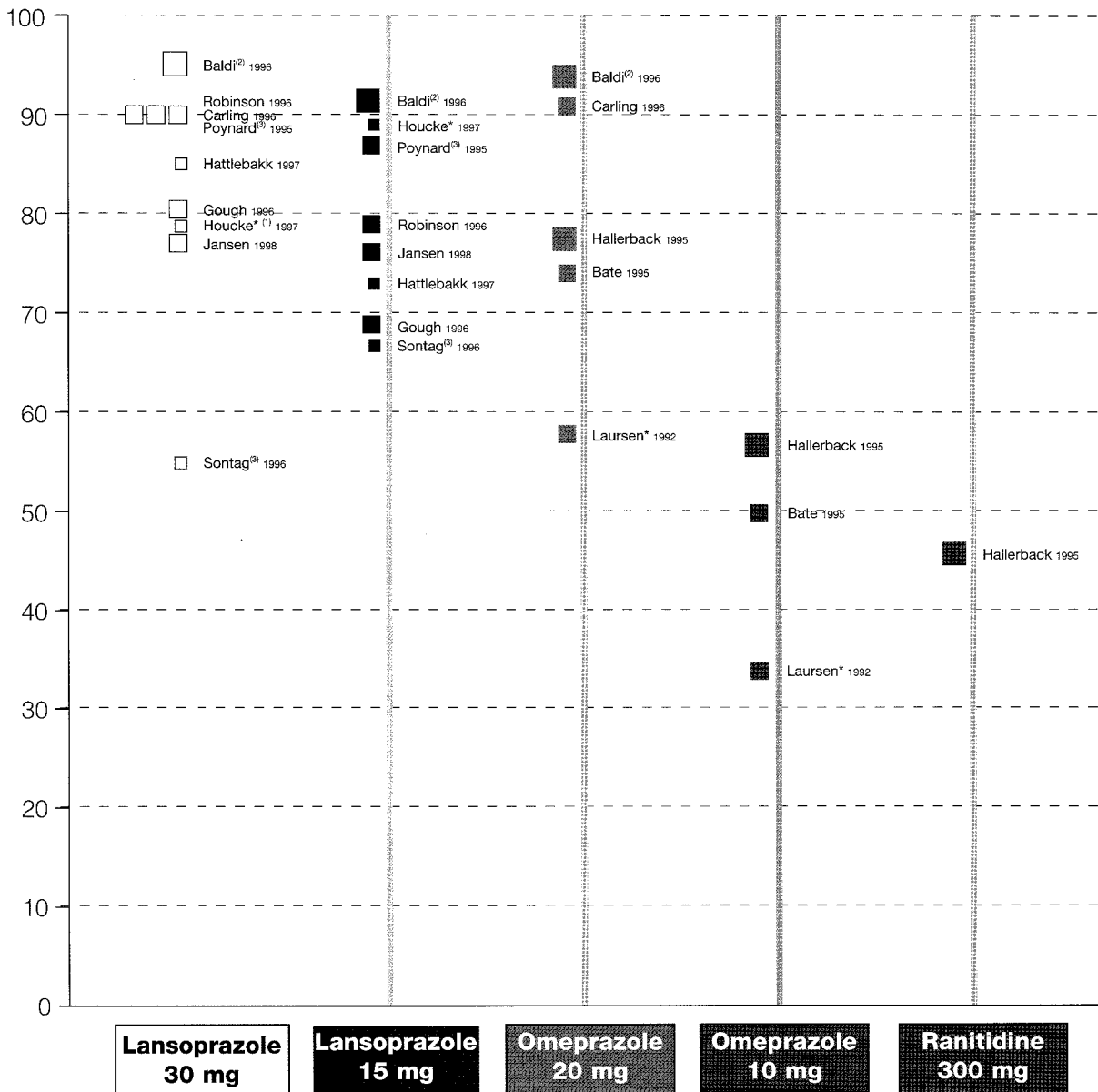
Intestinal transplantation might be considered in long-term HPN patients with metabolic complications or lack of vascular access.

References

1. SHILS M.E., WRIGHT W.L., TURNBULL A. *et al.* Long-term parenteral nutrition through external arteriovenous shunt. *New Engl. J. Med.*, 1970, **283**: 341-344.
2. JEEJEBHOY K.N., ZOHRAB W., LANGER B. *et al.* Total parenteral nutrition at home for 23 months, without complication and with good rehabilitation. *Gastroenterology*, 1973, **65**: 811-820.
3. FLEMING C.R., Mc GILL D.B., BERKNER S. Home parenteral nutrition as primary therapy in patients with extensive Crohn's disease of the bowel and malnutrition. *Gastroenterology*, 1977, **73**: 1077-1081.
4. SOLASSOL C., JOYEUX H. Ambulatory PN. In: MANNI C., MAGALINI S., SCRASCIA E. (eds.), Parenteral Alimentation: The International Symposium on Intensive Therapy. New-York: American Elsevier, 1976, pp. 138-152.
5. HOWARD L., HEAPHEY L., FLEMING R., LININGER L., STEIGER E. Four years of North American Registry HPN outcome data and their implications for patient management. *JPEN*, 1991, **15**: 384-393.
6. HOWARD L., AMENT M., FLEMING R., SHIKE M., STEIGER E. Current use and clinical outcome of home parenteral and enteral nutrition therapies in the United States. *Gastroenterology*, 1995, **109**: 355-365.

ENDOSCOPIC REMISSION (%) AFTER 6 MONTHS OR 1 YEAR

Doubleblind studies (PPI versus active comparator)
in maintenance treatment of RO grade I-IV



* after 6 months

(1) Lansoprazole 30 mg once every two days

(2) Patients with compliance $\geq 80\%$

(3) H₂RA-resistant

■ n > 300 ■ 150 < n < 300 ■ n < 150

Baldi F. et al. - Gastroenterology 1996 Apr; 110 (4) Suppl.: A55, Poster • Bate CM. et al. - Gut 1995; 36: 492-498 • Carling L. et al. - Gut 1996; 39 (Suppl.3): A182, 1036 • Gough AL. et al. - Aliment Pharmacol Ther 1996; 10: 529-539 • Hallerback B. et al. - Gastroenterology 1994; 107 (5): 1305-1311 • Hattlebakk JG. & Berstad A. - Gastroenterology 1995; 108 (4, Suppl.): A111 • Houcke Ph. et al. - Gastroenterology 1997; 112 (4, Suppl.): A152 • Jansen J. et al. - Gastroenterol 1998; 114 (4) part 2, A160 • Laursen LS. et al. - Scand J Gastroenterol 1995; 30 (9): 839-846 • Poynard T. et al. - Gastroenterology 1995; 108 (4, Suppl.): A195 • Robinson M. et al. - Ann Intern Med 1996; 124 (10): 859-867 • Sontag SJ. et al. - Am J Gastroenterol 1996; 91 (9): 1758-1765

60. LEWIS J., LAFRANCE R., BOWER R. Treatment of infected silicone right atrial catheter with combined fibrinolytic and antibiotic therapy: Case report and review of the literature. *JPEN*, 1989, **13**: 92-98.
61. BEERS T R., BURNES J., FLEMING C.R. Superior vena caval obstruction in patients with gut failure receiving home parenteral nutrition. *JPEN*, 1990, **14**: 474-479.
62. BUCHMAN A.L., MOUKARZEL A., AMENT M.E. *et al.* Catheter thrombosis and SVC/IVC syndrome are rare complications of long-term TPN. *Clin. Nutr.*, 1994, **13**: 356-360.
63. FORBES S.C.D., COURTNEY J.M. Thrombosis and artificial surfaces. In: BLOOM L., THOMAS D. (eds). Haemostasis and thrombosis. Edinburgh: Churchill Livingstone, 1987, pp. 902-921.
64. WAKEFIELD A., COHEN Z., CRAIG M. *et al.* Thrombogenicity of total PN solutions: effect on induction of monocyte/macrophage pro-coagulant activity. *Gastroenterology*, 1989, **97**: 1210-1219.
65. DI CONSTANZO J., CANO N., VADON D., VADON M. Venous thrombosis during total parenteral nutrition with central venous catheter: role of nutritive solutions. *Clin. Nutr.*, 1982, **1**: 201-205.
66. PITHIE A., SOUTAR S., PENNINGTON C. Catheter tip position in central venous thrombosis. *JPEN*, 1988, **12**: 613-614.
67. LINDER L., CURELARU I., GUSTAVSSON B. *et al.* Material thrombogenicity in central venous catheterisation: a comparison between soft antebraichal catheters of silicone elastomer and polyurethane. *JPEN*, 1984, **8**: 399-406.
68. VEERABAGU M., NEWHALL J., MALIAKKAL R., CHAMPAGNE C., MASCIOLI E. Warfarin and reduced central venous thrombosis in home total parenteral nutrition patients. *Nutrition*, 1995, **11**: 142-144.
69. FARRI P., MIRTALLO J., RUBERG R., *et al.* Incidence and prevention of thrombosis of subclavian vein. *Surg. Gynecol. Obstet.*, 1982, **155**: 238-240.
70. BERN M., LOCKICH J., WALLACH S., *et al.* Very low doses of Warfarin can prevent thrombosis in central venous catheters. *Ann. Int. Med.*, 1990, **112**: 423-428.
71. DUERKSEN D., AHMAD A., DOWEIKO J., BISTRIAN B., MASCIOLI E. Risk of symptomatic central venous thrombotic complications in AIDS patients receiving home parenteral nutrition. *JPEN*, 1996, **20**: 302-305.
72. PITHIE A., PENNINGTON C. Incidence, aetiology and management of central vein thrombosis during parenteral nutrition. *Clin. Nutr.*, 1987, **6**: 151-153.
73. BARCLAY G., PENNINGTON C. Tissue plasminogen activator in the management of superior vena cava thrombosis associated with parenteral nutrition. *Postgrad. Med. J.*, 1990, **66**: 398-400.
74. ROSENBLUM J., LEEF J., MEUERSMITH R., TOMIAK M., BECK F. Intravascular stents in the management of acute superior vena cava obstruction of benign aetiology. *JPEN*, 1994, **18**: 362-366.
75. GLYN M., LANGER B., JEEJEEBHOY K.N. Therapy of thrombotic occlusion of long-term intravenous alimentation catheters. *JPEN*, 1980, **4**: 387-390.
76. LEREBOURS E., DUCABLE G., FRANCHESCHI A., SAOUR N., COLIN R. Catheter obstruction during prolonged parenteral alimentation: are lipids responsible? *Clin. Nutr.*, 1985, **4**: 135-138.
77. BEAU P., MATUCHANSKY C. Lipid delivery and catheter obstruction during cyclic total PN. *Lancet*, 1987, **330**: 1095-1096.
78. RICHARDS D., DEEKS J., SHELDON T., SHAFFER J. Home parenteral nutrition. *Health Technol. Assess.*, 1997, **1** (1).
79. SHAFFER J. Hepatic complications of parenteral nutrition. *Clin. Nutr.*, 1995, **14** (suppl): 59-64.
80. LINDOR K., FLEMING C., ABRAMS A., HIRSCHKORN M. Liver function values in adults receiving total parenteral nutrition. *JAMA*, 1979, **241**: 2398-2400.
81. BOWYER B.A., FLEMING C.R., LUDWIG J., PETZ J., Mc GILL D.B. Does long-term home parenteral nutrition in adult patients cause chronic liver disease? *JPEN*, 1985, **9**: 11-17.
82. MESSING B., BITOUN A., GALIAN A., MARY J.Y., GOLL A., BERNIER J.J. La stéatose hépatique au cours de la nutrition parentérale dépend-elle de l'apport calorique glucidique? *Gastrointest. Clin. Biol.*, 1977, **1**: 1015-1025.
83. KEIM N. Nutritional effects of hepatic steatosis induced by parenteral nutrition in the rat. *JPEN*, 1987, **11**: 18-22.
84. LOWRY S., BRENNAN M. Abnormal liver function during parenteral nutrition relation to infusion excess. *J. Surg. Res.*, 1979, **26**: 300-307.
85. BUZBY G., MULLEN J., STEIN T., ROSATO E. Manipulation of TPN caloric substrate and fatty infiltration of the liver. *J. Surg. Res.*, 1981, **31**: 46-54.
86. PAPPO I., BERCOVIER H., BERRY E., GALLILLY R., FEIGIN E., FREUND H. Antitumor necrosis factor antibodies reduce hepatic steatosis during total parenteral nutrition and bowel rest in the rat. *JPEN*, 1995, **19**: 80-82.
87. SHELDON G., PETERSEN S., SANDERS R. Hepatic dysfunction during hyperalimentation. *Arch. Surg.*, 1978, **113**: 504-508.
88. MESSING B., DE OLIVEIRA F., GALIAN A., BERNIER J.J. Cholestase au cours de la nutrition parentérale totale mise en évidence de facteurs favorisants: association à une lithiase vésiculaire. *Gastroenterol. Clin. Biol.*, 1982, **6**: 740-747.
89. FOUIN-FORTUNET H., LE QUERNEC L., ERLINGER S., LEREBOURS E., COLIN R. Hepatic alterations during total parenteral nutrition in patients with inflammatory bowel disease: a possible consequence of lithocholate toxicity. *Gastroenterology*, 1982, **82**: 932-937.
90. STANKO R., NATHAN G., MENDELOW H., ADIBI S. Development of hepatic cholestasis and fibrosis in patients with massive loss of intestine supported by prolonged parenteral nutrition. *Gastroenterology*, 1987, **92**: 197-202.
91. CARPENTIER V., RICHELLE M., HAUMONT D., DECKELBAUM R. New developments in fat emulsions. *Proc. Nutr. Soc.*, 1990, **49**: 375-380.
92. DE LEDINGHEN V., BEAU P., MANNANT D., INGRAND P. Parenteral nutrition-related liver disease and lipid emulsions containing medium chain triglycerides. *Clin. Nutr.*, 1995, **14** (2): 62 (abstract).
93. BEAU P., LABAT-LABOURDETTE J., INGRAND P., BEAUCHANT M. Is ursodeoxycholic acid an effective therapy for total parenteral nutrition-related liver disease? *J. Hepatology*, 1994, **20**: 240-244.
94. MESSING B., BORIES C., KUNSTLINGER F., BERNIER J.J. Does total PN induce gallbladder sludge formation and lithiasis. *Gastroenterology*, 1983, **84**: 1012-1019.
95. MESSING B. Gallbladder sludge and lithiasis: complications of bowel rest. *Nutrition*, 1990, **6**: 190-196.
96. LIPKIN E.W., OTT S.M., CHESNUT C.H. *et al.* Mineral loss in the parenteral nutrition patient. *Am. J. Clin. Nutr.*, 1988, **47**: 515-523.
97. SHIKE M., SHILS M.E., HELLER A. *et al.* Bone disease in prolonged parenteral nutrition: osteopenia without mineralization defect. *Am. J. Clin. Nutr.*, 1986, **44**: 89-98.
98. LIPKIN E.W., OTT S.M., KLEIN G.L. Heterogeneity of bone histology in parenteral nutrition patients. *Am. J. Clin. Nutr.*, 1987, **46**: 673-680.
99. EPSTEIN S., TRABERG H., LEVINE G. *et al.* Bone and mineral status of patients beginning parenteral nutrition. *JPEN*, 1986, **10**: 263-264.
100. DE VERNEJOU M.C., MESSING B., MODROWSKI D. *et al.* Multifactorial low remodeling bone disease during cyclic total parenteral nutrition. *J. Clin. Endocrinol. Metab.*, 1985, **60**: 109-113.
101. KOO W.W., KAPLAN L.A. Aluminium and bone disorders: with specific references to aluminium contamination of infant nutrients. *J. Am. Coll. Nutr.*, 1988, **7**: 199-214.
102. VARGAS J.H., KLEIN G.L., AMENT M.E. *et al.* Metabolic bone disease of total parenteral nutrition: course after casein to amino acids in parenteral solutions with reduced aluminium content. *Am. J. Clin. Nutr.*, 1988, **48**: 1070-1078.
103. LIPKIN E.W., OTT S.M., KLEIN G.L. Serum markers of bone formation in parenteral nutrition patients. *Calcif. Tissue Int.*, 1990, **47**: 75-81.
104. SAITTA J.C., OTT S.M., SHERRARD D.J., WALDEN C.E., LIPKIN E.W. Metabolic bone disease in adults receiving long-term parenteral nutrition: longitudinal study with regional densitometry and bone biopsy. *JPEN*, 1993, **17**: 214-219.
105. STAUN M., TJELLESEN L., THALE M. *et al.* Bone mineral content in patients on home parenteral nutrition. *Clin. Nutr.*, 1994, **13**: 351-355.
106. FOLDES J., RIMON B., MUGGIA-SULLAM M. *et al.* Progressive bone loss during long-term home parenteral nutrition. *JPEN*, 1990, **14**: 139-142.
107. VERHAGE A.H., CHEONG W.K., ALLARD J.P., JEEJEEBHOY K.N. Increase in lumbar spine bone mineral content in patients on long-term total parenteral nutrition without vitamin D supplementation. *JPEN*, 1995, **19**: 431-436.
108. SHAFFER J., the ESPEN-HAN group. A European survey on management of metabolic complications in home parenteral nutrition. *Clin. Nutr.*, 1997 (abstract).
109. MAIN A., HULL M., MUSSELL R., *et al.* Clinical experience of zinc supplementation during intravenous nutrition in Crohn's disease: value of serum and urine zinc measurement. *GUT*, 1982, **23**: 984-991.
110. RANNEM T., LADEFOGED K., HYLANDER E. *et al.* Selenium depletion in patients on home parenteral nutrition. The effect of selenium supplementation. *Biol. Trace Elem. Research*, 1993, **39**: 81-90.
111. JEEJEEBHOY K.N., CHU R., MARLISS E. *et al.* Chromium deficiency, glucose intolerance and neuropathy reversed by chromium supplement-

- tation, in a patient receiving long-term total parenteral nutrition. *Am. J. Clin. Nutr.*, 1977, **30** : 531-538.
112. VERHAGE A., CHEONG W., JEEJEEBHROY K.N. Neurologic symptoms due to possible chromium deficiency in long-term parenteral nutrition that closely mimic metronidazole-induced syndromes. *JPEN*, 1996, **20** : 123-127.
113. EJIMA A., IMAMURA T., NAKAMURA S. *et al.* Manganese intoxication during total parenteral nutrition. *Lancet*, 1992, **339** : 426.
114. ALVES G., THIEBOT J., TRACQUI A. *et al.* Neurologic disorders due to brain manganese deposition in a jaundiced patients receiving long-term parenteral nutrition. *JPEN*, 1997, **21** : 41-45.
115. BROWN R., HAMRICK K., DICKERSON R. *et al.* Hyperkalemia secondary to concurrent pharmacotherapy in a patient receiving home parenteral nutrition. *JPEN*, 1996, **20** : 429-432.
116. MESSING B., LEMANN M., LANDAIS P. *et al.* Prognosis of patients with non-malignant chronic intestinal failure receiving long-term home parenteral nutrition. *Gastroenterology*, 1995, **108** : 1005-1010.
117. AUGUST P., THORN D., FISHER R., WELCHEK C. HPN for patients with inoperable malignant bowel obstruction. *JPEN*, 1991, **15** : 323-327.
118. HOWARD L. Home parenteral and enteral nutrition in cancer patients. *Cancer*, 1993, **72** : 3531-3541.
119. MESSING B., LANDAIS P., GOLDFARB B. *et al.* Nutrition parentérale à domicile chez l'adulte : résultats d'une enquête multicentrique en France. *Presse Médicale*, 1988, **17** : 845-849.
120. BYRNE T., PERSINGER R., YOUNG L., *et al.* A new treatment for patients with short-bowel syndrome. Growth hormone, Glutamine, and a modified diet. *Ann. Surgery*, 1995, **222** : 243-245.
121. CARLSON G.L., MAGUIRE G., WILLIAMS N., BRADLEY A., SHAFFER J.L., IRVING M. Quality of life on home parenteral nutrition and attitudes towards intestinal transplantation. A single centre study of 37 patients. *Clin. Nutr.* (in press).
122. SMITH C.E. Quality of life in long-term total parenteral nutrition patients and their family caregivers. *JPEN*, 1993, **17** : 501-506.
123. RICHARDS D., IRVING M. Assessing the quality of life of patients with intestinal failure on home parenteral nutrition. *Gut*, 1997, **40** : 218-222.
124. BOULETREAU P., GERARD M., MESSING B., *et al.* Home parenteral nutrition and AIDS. *Clin. Nutr.*, 1995, **14** : 213-218.
125. WILCOCK H., ARMSTRONG J., COTTEE S., NEALE G., ELIA M. Artificial nutritional support for the patients in the Cambridge health district. *Health Trends*, 1991, **23** : 93-100.
126. MASLOW K. Total parenteral nutrition and tube feeding for elderly patients : findings of an OTA study. *JPEN*, 1988, **12** : 425.