

## Lessons from a 20 year experience of Home Parenteral Nutrition in adult patients

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### Abstract

**Background :** Home Parenteral Nutrition (HPN) is a method commonly used in patients with Chronic Intestinal Failure (CII) related to benign or malignant diseases. We report the experience from a 20 year programme of HPN in a single academic centre.

**Methods :** In this study, we have reviewed characteristics and outcome of a group of patients enrolled in a HPN program between 1987 and 2007. Focus was given to the prevalence and severity of cholestasis in these patients as well as on their oral food behaviour.

**Results :** In 20 years, 125 patients were included in a HPN programme ; 65 patients had benign diseases (BD) and 60 advanced cancer (AC). Short bowel was the most common indications in patients with BD. Almost 40% of patients with BD were weaned off HPN. Median survival was excellent in BD patients and extremely short in AC. Death related to HPN was very rare. Cholestasis has been observed in 84% of patients but it was mild to moderate in the majority of cases. Hyperphagia was observed in 50% of the patients with BD on long-term HPN.

**Conclusions :** This study confirms that HPN is the first line therapy in CII due to BD. Patients with AC should be carefully selected. Cholestasis is frequent but mostly without clinical impact. Half of the patients with CII due to BD become hyperphagic allowing to reduction of parenteral intake. The role of a multi-disciplinary nutrition support team is essential for optimizing HPN. (*Acta gastroenterol. belg.*, 2010, 73, 451-456).

**Key words :** parenteral nutrition, home parenteral nutrition, intestinal failure, short bowel, hyperphagia.

### Introduction

The use of Home Parenteral Nutrition (HPN) started in Europe and United States in the early seventies (1). The first experience was reported by Shils *et al.* in 1967 who managed to maintain a patient on HPN for a few months (2). Since then, the central venous line providing parenteral nutrition was considered as the “artificial gut” (3). In Belgium, some patients were on HPN in the early eighties ; thereafter, a dedicated programme for HPN in adult patients was first launched in Erasme Hospital (Brussels) in 1987. The Nutritional Support Team (NST) in our institution engaged in the HPN program progressively included physicians, one pharmacist, two pharmacy technicians, one dietician and one clinical nutrition nurse.

Initially, HPN was exclusively reserved for patients with chronic intestinal failure (CII) related to benign underlying diseases such as Crohn’s disease or mesenteric infarction (1,4).

Intestinal failure is defined as a reduced intestinal absorption so that macronutrient and/or water and electrolyte supplements are needed to maintain health

and/or growth (5). It results from obstruction, dysmotility, surgical resection, congenital defect or disease-associated loss of absorption and is characterized by the inability to maintain protein-energy, fluid, electrolyte or micronutrient balance (6).

Since 1990, HPN has been increasingly used in patients with intestinal failure due to an advanced cancer, causing intestinal obstruction mainly due to extended carcinomatosis. Since then, cancer has become a major HPN indication in US but also in Europe (7-9).

The administration of HPN carries the risk of some complications ; either metabolic or related to central intravenous line (4). We also have to take into consideration psychological disturbances as well as difficulty of social adaptation (10). Nevertheless, in majority of patients with chronic intestinal failure due to a benign disease, HPN can offer a good quality of life (11,12).

Among metabolic complications, hepatobiliary dysfunction is the most common complication (4,13-14). The most frequent biochemical abnormality observed in HPN patient is cholestasis while a great number of histological varieties have been observed in this situation (13,15). Chronic cholestasis is defined as an increase in alkaline phosphatase (ALP) levels more than once within six months (16). The cause of chronic cholestasis is multifactorial ; in some patients liver abnormalities may lead to an irreversible chronic liver disease. In this situation only intestinal transplantation could be curative (15).

Preserving oral food intake in patients with chronic intestinal failure on HPN may have a protective effect by avoiding hepatic alteration (14,17). Some HPN patients become hyperphagic (18). Providing appropriate diet counselling is important in these patients (19).

In this work, we report the 20 year experience of HPN in our centre, focusing on indications and outcome, the

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incidence and severity of cholestasis, as well as the oral food behaviour of the HPN patients.

## Material and methods

This work contains three parts :

1) First, we report the 20 year experience of patients on HPN in our centre from 1987 to 2007. The following parameters were retrospectively reviewed : number of patients/year ; age ; gender ; indications for HPN ; underlying diseases (Crohn's disease, mesenteric infarction, radiation enteritis, post-surgery, miscellaneous) ; the anatomic characteristics of the remaining gut in case of short bowel : type 1 = terminal enterostomy, type 2 = jejunocolic anastomosis, type 3 = jejunoleal anastomosis (20) ; the type of cancer for malignant diseases ; duration of HPN ; mean number of bags per week ; outcome (weaning, death, ongoing) ; cause of death ; incidence of central venous catheter related septic episodes and candidate for intestinal transplantation.

2) The second part is dedicated to the prevalence, duration and severity of biochemical cholestasis in HPN patients. Cholestasis has been divided into three groups upon the degree of severity (21) :

A-Mild chronic cholestasis defined as an ALP concentration less than twice the normal value.

B-Moderated chronic cholestasis defined as an ALP concentration between twice the normal rate and five times the normal rate.

C-Severe chronic cholestasis defined as ALP concentration more than five times the normal rate.

3) The third part of this work focuses on the oral food behaviour of patients on HPN. The results have been obtained through a dietetic inquiry in the form of a questionnaire. The patients have been questioned either at the hospital or in their house. In this way, a dietary recall over one week was established. Dietary intake measurement based on food frequency questionnaire were established and analyzed through a nutritional software program, "Nutrilog" (<http://www.nutrilog.com>). Upon the fact that the patients were under parenteral once per day or not, they had a second questionnaire "24 hr reminder", in order to be able to evaluate their alimentary habits and appetite. Hyperphagia was defined when oral food intake values were higher ( $1.5 \times$ ) than the patient's needs, calculated on basis of the Harris-Benedict formula (18).

## Statistical analysis

Descriptive statistics are expressed in mean or median for continuous values. Comparisons were done using the t-test for continuous values and the chi-square test for categorical values. Correlations were performed using the Spearman test.

Statistical significance was considered for p values  $\leq 0.05$ . Statistical analyses were performed using SPSS software, version 11.0 (SPSS Inc., Chicago, IL).

## Results

### Patient characteristics and outcome

Between January 1987 and January 2007, 125 adult patients were included in our HPN program at Erasme Hospital. Fifty-five percent (65 patients) had benign pathologies and the remaining patients were suffering from different types of cancer.

### Patients with benign diseases

In patients with benign underlying diseases ; there were 35 females and 30 males with a median age of 52 at the beginning of HPN. The underlying diseases among patients with benign diseases were : Crohn's disease in 24%, mesenteric vascular disorder in 32%, radiation enteritis in 4%, post surgical complications in 15% and 25% of the patients were suffering from other pathologies. In this last group (16 patients), we had one HIV positive patient suffering from severe malnutrition, 2 patients with immunologic disorders, 1 case of cystic fibrosis, 2 pulmonary transplants patients, 2 cases of chronic pancreatitis and 6 patients with intestinal motor disorders.

Among Crohn's patients, 13 had a short bowel syndrome and the three others had fistulas. All patients with mesenteric infarction had a short bowel syndrome. The 3 patients with radiation enteropathy had malabsorption. Among post-surgical cases we had one short bowel syndrome and one case of malabsorption (Table 1). Among patients with a short bowel ( $n = 42$ ), 15 had a type I, 25 a type II and 2 a type III anastomosis.

The cumulative duration of HPN in patients with benign conditions was 2492 months (from 1 to 240 months), corresponding to 74,760 days and administration of 45,444 bags. The median duration of HPN regarding underlying diseases is given on Table 2.

In January 2005 there were two potential candidates for intestinal transplantation among the 23 patients who were currently on HPN. They both had Crohn's disease and were under HPN for 84 and 48 months respectively. These 2 patients were included in large Cohort of HPN patients in Europe for a long term follow-up.

The global outcome of patients was different according to the underlying disease. Among patients with Crohn's disease, 62% were weaned off HPN, 25% continued and 13% died at the time of evaluation ; in patients with mesenteric infarction, 19% were weaned off, 63% died and 19% continued, respectively. Overall, in 65 patients with benign diseases on HPN, 40% died, 35% were weaned off and 25% continued. For 26 patients who died, the death was related to the underlying diseases in 15, to HPN in 3 (2 patients with liver failure and one with central venous catheter sepsis), and 2 cases of suicide (in one patient due to the progressive motility disorder that was associated with neurological alteration and one case of primary psychiatric disorder not related to HPN).

Table 1. — Indications for HPN regarding various underlying diseases

	HPN in patients with benign diseases (n = 65)				
	Crohn N = 16	Mesenteric N = 21	Radiation N = 3	Post-surgery N = 9	Miscellaneous N = 16
Short bowel	13	21	—	8	—
Fistula	3	—	—	—	—
Malabsorption	—	—	3	1	16

Table 2. — Duration of HPN regarding various underlying diseases

	HPN in patients with benign diseases Duration				
	Crohn N = 16	Mesenteric N = 21	Radiation N = 3	Post-surgery N = 9	Miscellaneous N = 16
n	16	21	3	9	16
Total	826	718	138	213	597
Months (average)	51 (1-240)	34 (1-120)	46 (3-120)	24 (1-120)	37 (1-144)

#### Patients with malignancy

Cancer has been the main indication of initiating HPN in 45% of our patients. Median age was 56 years. In this category we found 21 patients with gastric cancer, 16 patients with other GI cancer, 9 women with an ovarian cancer, 3 with other gynaecological cancers and 11 patients with a non GI and non-gynaecological related neoplasia.

Among 60 cancerous patients under HPN, 59 died and there was a transient weaning off in one patient suffering from ovarian cancer. The median survival rate in patients with ovarian cancer was 63 days, 49 days in patients with gastric neoplasia and 35 days in non gastric cancerous group, respectively. The survival duration in this population is described in Figure 1.

#### Complications

##### Infectious complication

In our series, we observed 18 episodes of central venous catheter line-related sepsis in patients with Crohn's disease with a median duration of 51 months (this corresponds to one infection every 32 months). In patients suffering from mesenteric infarction with a mean duration of 41 months, there were 15 cases of sepsis (one infection per 44.5 month of HPN), and we observed 9 episodes in the other categories (one episode every 37 months).

##### Cholestasis and HPN

We had a long term follow-up in 26 patients (14 male and 12 female) who were on HPN from 28 months to 240 months. The prevalence of chronic cholestasis in patients on HPN was 84%. The severity of cholestasis was classified as mild in 27%, moderate in 59% and severe in 13% respectively. In 95% of cases cholestasis

#### HPN in cancer patients Survival

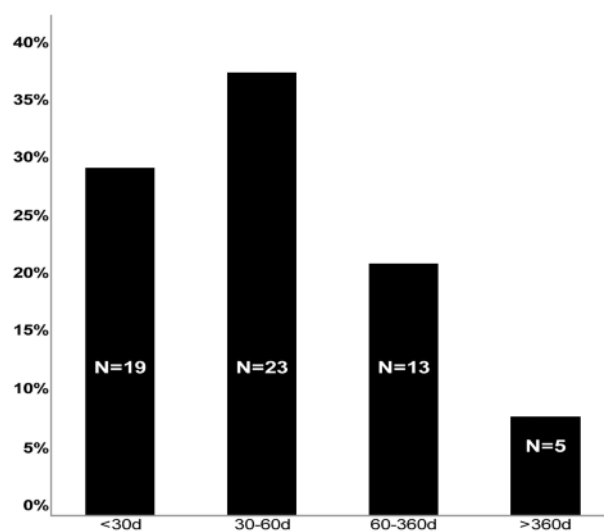


Fig. 1. — Survival of patients with advanced cancer on Home Parenteral Nutrition (HPN).

was not complicated. Cholestasis was more frequent in patients with short bowel (93.3% vs 72.7%, NS). All the patients with an enterostomy had cholestasis. Interestingly, the degree of severity remained stable in all but 3 patients in whom we observed a progressive increase in the level of ALP.

There was no correlation between the degree of chronic cholestasis and the underlying disease. Interestingly we observed a significant correlation between serum C-Reactive Protein (CRP) levels and the level of ALP ( $p = 0.02$ ). In this group of 26 patients we

observed 8 episodes of hyperbilirubinemia that were all simultaneous to an episode of sepsis (in 7 out of 8 due to CVC line) and that rapidly resolved after controlling sepsis by adequate antibiotherapy.

#### *Oral intake behaviour*

17 patients were enrolled in this evaluation assessing the oral food intake. They were 7 females and 10 males. The duration of HPN was from 6 to 240 months. All but one patient had a short gut and 5 had an enterostomy. The mean parenteral intake was 1090 Kcal per day (350-1810 Kcal/day) and the oral intake was 2450 Kcal (320-7210 Kcal/day).

Only 1 out of 17 patients could not reach the recommended nutritional needs despite parenteral nutrition. In 12% (2 patients) the caloric intake was equivalent to their needs. We have observed that in 14 patients (82%) their total oral intake was more than their needs.

There was no correlation between oral alimentary intake and the number of nutritional bags used by patients each week. The caloric content of the nutritional bag (940-2520 Kcal/bag) had no influence on patients' oral intake. Among these 17 patients, 9 were considered to be hyperphagic ( $1.5 \times$ ). There was no influence of having a stoma or not.

## **Discussion**

This 20 year experience of HPN confirms that HPN is the first line therapy in patients with intestinal insufficiency related to benign disorders with an excellent long term survival. It also shows that HPN has a place in advanced cancer patients but requires a good selection. Moreover, biochemical cholestasis seems to be frequent in patients on HPN but rarely severe and that occurrence of cholestasis may be influenced by a chronic inflammation reflected by the serum CRP level and finally that a hyperphagic adaptation is observed in 50% of the cases. The last and probably the most important message of our experience is certainly the need of a multidisciplinary NST for optimizing the HPN programme and limiting the risk of complications.

The present work reports the 20 years experience of HPN performed in a single Belgian centre. Although the programme initially enrolled only patients with benign diseases we reported the use of HPN in cancer patients (45% of HPN population); such prevalence is similar to other European countries while there is some disparity throughout European countries (7-9). Indeed HPN is more commonly used for cancer patients in Italy than in UK (7). Such difference is due to cultural, sociological and medical approaches of patients with advanced cancer. Obviously the increasing use of HPN in patients with advanced cancer has several explanations: medical, with the development of multimodal cancer therapies but also economical pressure for discharging as soon as possible the patients from the hospitals. Moreover the cumulative

experience in HPN as well as the launching of Home Care services has also contributed to this trend. Decision of starting HPN in incurable cancer patients should be taken by the oncologist in collaboration with NST team (22,23). Advantages and disadvantages should be clearly described to the patient (24). Besides their inability to meet their nutritional requirements by oral or enteric route, cancer patients should have at least a Karnofsky score of higher than 50 and normally be free of liver and lung metastasis. According to ESPEN Guidelines, HPN is not recommended for cancer patients with a short life-expectancy (22). However, our experience shows that even with a strict selection of patients the survival time of 50% of these patients is extremely short. In some cases we have to accept that starting HPN was influenced by emotional and psychological parameters including the willing of the patient to die at home.

In patients with benign diseases the percentage of patients with Crohn's disease progressively decreased since the last decade. This is certainly due to the improvement of medical control of the inflammatory disease with the introduction of immunoregulation and new biological treatments.

Short bowel remains the main HPN indication in patients with benign disorders. In our series we collected only a few cases with dysmotility problems in comparison with the Paris experience (25); this is probably related to specific recruitment of these patients in some centres. Our experience fits with the ESPEN recommendations stating that HPN support should be used in patients who cannot meet their nutritional requirement by enteric intake, and who are able to receive therapy outside an acute care setting (22).

HPN duration was similar to other series with a weaning rate of nearly 40% (26). Weaning from HPN occurred within 2 years after starting in most of the patients. Indeed, although there are some reports of weaning after several years the process of adaptation seems to be reached within 24 months on HPN (22,26). HPN weaning depends on several adaptative mechanisms. First, adaptation of the residual intestine with villous hypertrophy is important. It is mandatory to determine not only the length of the remaining gut but also the type of short bowel. Indeed, the capacity of adaptation is better in case of type II and III than in case of enterostomy (type I) (20). Additionally, the colon has adaptative capacities if still in continuity. In fact it has been shown that colonic microbiota is likely to produce volatile short chain fatty acids (butyric and acetic acid) which are the preferred fuels for colonocytes, are partially reabsorbed and used as caloric sources for the body (17,18). Finally, the third adaptative mechanism is hyperphagia that we have confirmed in 50% of our patients (17). We should mention that in some cases surgical remodelling of the residual gut may contribute to an adaptation and subsequently to a weaning from HPN (27).

Joly *et al.* have recently shown that intestinal microbiota in patients with short bowel were completely



modified with a predominance of lactobacilli (28). Reasons and consequences of such colonic microbiota is unknown and needs further investigations.

In our series, several patients were requiring HPN for more than 10 years. During the last decade, only 2 patients were considered as potential candidates for intestinal transplantation based upon actual criteria. These patients were included in a large European study evaluating indications and percentages of HPN patients who were candidates for intestinal transplantation (29). The 3 year follow up of this unique European Cohort showed that HPN remains the first line therapy in chronic intestinal failure and provided information on the accuracy of the actual criteria for recommending intestinal transplantation (30).

In the present series the number of death related to HPN was very low as it has been previously reported (26). It seems that death related to the underlying diseases mostly occurred quite early while death due to HPN complications are observed after several years.

In our series central venous line infection was the most frequent complication related to HPN as previously reported (4,26). Nevertheless, the number of infectious episodes remained very low and we only observed one death due to a central venous line infection. A multidisciplinary approach, including the expertise of a consultant physician, pharmacists, dietician and especially a clinical nutritional specialist nurse is fundamental in order to limit the risk of infection (22). When a patient needs to be kept on HPN, the main goal is to provide the longer survival but also the best quality of life. In order to provide the best autonomy, the patient should be trained to perform the handling of the line by himself. Education of the patient is extremely important in order to avoid complications and especially CVC line infection. It is vital to thoroughly assess patients' physical and cognitive abilities as well as their social status before embarking in an HPN training program. If patient's education is not possible, a relative or a community nurse could fulfil this role. For educating and monitoring the patient and his family, the role of a specialized clinical nutrition nurse is fundamental (31).

Hepatobiliary diseases are considered as the most frequent and severe HPN complications (13,14). Absence of oral food intake, intravenous hyperalimentation, intravenous intake of lipid emulsion higher than  $> 1$  g/kg/day, remnant bowel of  $< 50$  cm, taurine deficiency, multiples strictures on the remnant bowel with bacterial overgrowth, phytosterolemia (13,14,16,32,33) are all factors associated with HPN liver disease. In our series we have examined the prevalence and the severity of cholestasis in long term HPN patients. We could confirm an increase of ALP in nearly 84% of our population. However, in majority of cases this cholestasis was mild to moderate (19,21). We also observed that cholestasis severity remains stable in the majority of cases. Our study showed a significant correlation between cholestasis and serum CRP levels. Several HPN patients had elevated

serum CRP without any obvious reasons. An association between a chronic inflammation and the risk of developing cholestasis and HPN associated liver disorders has been already reported (34). In our series the rare episodes of hyperbilirubinemia were always associated with sepsis mostly related to a CVC line infection. Only one of our patients died from liver failure. Indeed, hepatic failure is also rare in other published series (13,14,32,33). As shown in the European report, severe hepatic disease remains a major indication for dual liver-intestine graft (30). Meanwhile, the same study has shown that combined transplantation has a worse outcome. Therefore, prevention of liver disorders is essential. Different measures allows to decrease hepatic alterations : adequate amount of lipid and total caloric intake, prevention and rapid treatment of infectious episodes, withdrawal of hepatotoxic factors such as alcohol or drugs, prevention by vaccination or treatment of viral hepatitis according to general recommendations and finally maintaining oral food intake.

Our study has also focused on oral food intake in HPN patients. As it has been previously reported by Messing *et al.*, a significant percentage of HPN patients with oral food intake become hyperphagic (18). Oral food intake has not only a protective effect preserving intestinal mucosal trophicity but also allows diminishing intravenous intake. In patients with a remaining colon the role of a diet enriched in carbohydrates is mandatory in order to enhance the production of volatile short chain fatty acids which contributes to save up to 800 Kcal/day (17). The mechanism of this hyperphagic process is not totally understood but is probably driven by hormones such as leptin and ghrelin. This demonstrates the essential role of a specialist dietician within a NTS. Modification of parenteral energy intake should be done along with mechanisms of adaptation. When it is feasible regarding hydration and electrolytes balance, most of the patients preferred to limit the number of bags per week instead of diminishing the daily content of the bags. Such approach certainly contributes to improve their quality of life (12).

In conclusion, this 20 year experience shows the need of a multidisciplinary NST for selecting patients who could benefit from HPN, educating and monitoring patients for lowering complications and optimizing their life quality.

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