Home parenteral nutrition

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Introduction

Parenteral nutrition is the technique of providing the body’s nutritional requirements intravenously. The nutrients are water, glucose, electrolytes, amino acids, lipids, vitamins, minerals and trace metals. Home parenteral nutrition (HPN) is the method of administering this support at home. It is a technique which was developed just over two decades ago. Some infants and neonates who started on this technique in the mid 1970’s are now 18-20 years old. HPN is administered by parents or other caretakers of the child at home through an indwelling semi-permanent central venous catheter (CVC). HPN is supervised and monitored by a multi-disciplinary team consisting of physicians, nurses, pharmacists, dietitians (nutritionist) and social workers. This technique allows patients requiring long-term parenteral nutrition support to be cared for at home, thereby decreasing hospital stay, reducing the cost of care, promoting a near normal life style and avoiding complications associated with prolonged hospitalization.

Indications

Home parenteral nutrition is indicated in children requiring parenteral nutrition when normal growth and weight gain cannot be sustained through the enteral route. The patient should require HPN for at least thirty days to justify the training time and expense of establishing the patient on a HPN regimen. The common indications for HPN in children are listed in table I [1-12].

The most frequent indication in children is for management of short bowel syndrome, mainly small bowel resection due to neonatal necrotizing enterocolitis with infarction and congenital jejunooileal atresias. Ninety percent (90%) of children with more than 25 centimeters of functioning small bowel and an intact ileocaecal valve do not need long-term parenteral support [13]. Some children with an intact ileocaecal valve and as little as 10 cm of small bowel may, with time,
adapt completely to enteral feeds; they may, however, need prolonged parenteral support until such adaptation takes place [14]. Children with less than 10 cm of small bowel or primary or secondary motility disorders of the intestine may require parenteral support indefinitely. Long-term or life-long HPN may be needed in children with severe small intestinal mucosal injury from infection, gastrointestinal allergy, coeliac sprue in crisis with intractable diarrhoea or microvillous inclusion disease. Prolonged HPN support may also be required in children with intractable Crohn’s disease to induce remission.

Oncology patients may also need HPN support. The commonest indication in these children is graft-versus-host (GVH) disease affecting the small intestinal mucosa after bone marrow transplantation. HPN allows these patients to be discharged home while the GVH is brought under control. Patients with severe nausea and vomiting secondary to chemotherapy, bowel obstruction due to malignancy or malignancy induced malnutrition may also need HPN support. We have also supported patients with dysgammaglobulinaemia and immune deficient enterocolitis for years successfully with no apparent greater risk of infection.

Growth failure and malnutrition are common in infants with chronic liver disease awaiting orthotopic liver transplantation. A bigger child can receive a larger graft which is more readily available and carries less chance of vascular or biliary complications. We supplement some of these infants with parenteral support to promote and maintain growth. Children with AIDS, intractable diarrhoea and malnutrition may also require HPN support.

There is no absolute contraindication to HPN. However, at least one family member or caretaker must be motivated to be responsible for the daily tasks of HPN and respond to emergencies and problems associated with it.

**Venous access**

Percutaneous catheter insertion should be done under aseptic surgical conditions. Special attention should be paid to skin preparation with Povidone-iodine or chlorhexidine and alcohol [15, 16]. Studies suggest that antibiotic ointments are of no extra benefit if the catheter insertion site is properly cleaned [17]. In some catheters a temporary dissolvable silver nitrate impregnated cuff may reduce bacterial colonization at the exit site in the immediate post catheter placement period but does not decrease sepsis [18]. The infraclavicular subclavian vein is the commonest site for percutaneous catheter insertion. The tip of the catheter should be in the superior vena cava, near but not in the right atrium, ideally at the junction. The exit site is on the anterior chest wall. This has the advantage of allowing easy mobility of the patient and ease of keeping the exit site contamination free. Internal jugular or brachiocephalic veins are also used to gain access to the superior vena cava. The catheter is brought out to the anterior chest wall through a subcutaneous tunnel. Catheters can also be placed through the saphenous and femoral veins into the inferior vena cava. The tip of the catheter should be at, or just below, the level of the renal veins. In difficult cases, radiologically guided placement of CVC into the inferior vena cava has been done through the lumbar, azygos or hepatic veins [19]. Magnetic resonance angiography is an excellent way to evaluate the patency of possible access sites before catheter placement in patients with an access problem. Such patients may need thoracotomy and direct placement of the catheter in the superior vena cava. However, we have rarely faced this problem in children in our experience of more than two decades.

The protocol for cleaning the CVC exit site varies. We recommend that the exit site be cleaned daily and fresh sterile dressings be applied [20]. Sterile transparent semipermeable dressings, changed at a less frequent interval, have also been used but may have a slightly higher chance of infection [21]. CVCs can last from a few days to decades. The average life of CVCs in paediatric patients is about two years in our programme [22]. Common indications for removal are uncontrolled line infection, thrombosis, mechanical damage beyond repair and catheter migration. In growing children, position of the tip of the CVC should be checked once a year as it may migrate proximally and the catheter may need replacement. If the catheter is not easily removable due to fibrosis, it should be left in place rather than risking complications with forcible removal.

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Initiation of home parenteral nutrition

Training, motivation and involvement of the family are the most important factors for a successful HPN programme. The multidisciplinary team should offer continuing support and monitoring since HPN places major responsibility and stress on the family. Physicians initiating the HPN should discuss with the parents and other family members likely to be involved the nature of the patient’s illness, the need and expected duration of HPN, the responsibility of the family and possible complications. Realistic goals should be set and one or two caretakers should be identified based on the assessed motivation, intelligence and reliability. They should then be trained by a nurse in the daily procedures, asepsis, monitoring and appropriate responses to emergencies and complications associated with HPN. In our programme, parents take about 10 days to master these techniques. However, individual variations exist. The patient should not be discharged home till the HPN team is satisfied with the training of the caretakers. In each subsequent admission these protocols should be reviewed and reinforced.

Making and formulating the solution

The solution should be prepared in aseptic conditions using laminar flow hoods and double filtration to prevent passage of microorganisms and particulate matters into the solution. Batches of solutions should be routinely cultured for aerobes, anaerobes and fungi and tested for pyrogen before dispensing to the patient. Most of the time, HPN is a continuation of parenteral nutrition initiated at a hospital. This provides a chance to individualize the solutions to meet patient’s needs. However, to be cost effective, we use standard solutions whenever possible. The energy needs of the individual can be calculated from the height, weight and age but, in chronically malnourished patients, factors such as ideal weight for height and parental height and weight need to be considered in calculating energy needs. In difficult situations, indirect calorimetry is an excellent tool for determining the energy needs of the patient.

The concentration of glucose depends on the fluid needs of the patient. Though we commonly use 20% dextrose, more concentrated formulas can be used in children with restricted fluid intake. Glucose tolerance on parenteral nutrition should be established before discharge. Some patients with hyperglycaemia may require regular insulin (10 units for every 10 g of dextrose per liter) added to the parenteral solution. In our experience, however, children rarely need insulin at home.

We try to provide 20-30% of energy needs of the subject from fat in the form of 20% fat emulsion (Intralipid®). Lipid tolerance (serum triglyceride level below 200 mg/dl 6 hours after lipid infusion) should be documented before the patient goes home. The total dose of lipid should be kept below 3 g/kg to avoid lipid overload syndrome.

We use infant amino acid formula (Trophamine®) for infants and children below two years of age and balanced amino acid solutions for older children. The concentration of amino acids can be changed depending on the fluid intake of the patient. However, we use standard concentrations whenever possible. Children with protein losing enteropathy or other catabolic states may require more protein.

We add an H2 blocker (Famotidine®, 1 mg/kg) to the HPN solution in some patients to reduce amino acid infusion associated gastric acid secretion which may help reduce enterostomy output and diarrhoea in children with short bowel syndrome.

We do not recommend “3 in 1” solutions (dextrose, amino acids and lipid mixed in the same bag) for paediatric HPN as they may increase the risk of venous thrombosis and have been associated with pulmonary emboli [23]. Moreover, catheter life has been markedly shortened in children receiving these mixtures [24].

Infusion

The caretaker should be taught techniques of adding additives, such as H2 blockers, multivitamin solutions and other medications in an aseptic fashion, to the bag containing HPN solution. Utmost aseptic precautions should be taken during opening and closing the CVC while starting or ending HPN infusion. We recommend thorough
hand washing but not sterile gloves. We recommend scrubbing with six each of Povidone-iodine and alcohol swabsticks. In our opinion, physical scrubbing of the catheter cap and the adjacent area is an important factor in preventing infection. Disposable tubing should be used for each infusion. Connection between the tubing and the CVC can be made with simple needles, needle access secured with Click Lock® or with the newer needleless access system. However, the needleless access system may have an increased risk of line infection [25].

The patient is started on parenteral infusion round the clock in the hospital. Once serum electrolytes, formulation and volume have stabilized, we compress the infusion time by 1-2 hours per day, depending on the subject’s age. Total volume of the infusate is kept the same. Blood glucose level is monitored hourly for 4 hours after stopping parenteral nutrition and just before restarting. Infants below 6 months of age with little enteral intake should be infused over 16 hours at home. Between 6 months and 1 year of age, the infusion time may be reduced to 12 hours. School age children often tolerate infusion over 8 to 10 hours, thereby setting the evening free for other activities. At the end of infusion, the rate is gradually decreased and stopped over 30 minutes to 1 hour to decrease the chance of reactive hypoglycaemia. Although some studies indicate that abrupt stoppage of parenteral infusion in children over 2 years of age is not associated with hypoglycaemia [26], we have not found it to be true and recommend gradual weaning described above.

Infusion pumps are required for HPN administration. The caretaker is trained in programming and using the pump. A representative of the manufacturer of the pump or the HPN provider should be available round the clock in case of pump malfunction. A portable pump that fits into a backpack is also available for exceptional children who require a prolonged infusion time.

Discharge and follow-up care

Before discharging a patient on HPN, logistics of supplying and storing the HPN supplies should be established. Most families receive their solutions pre-mixed, delivered at home at an interval of 2 days to 4 weeks, depending on the supplying agency and storage capability. Indeed, enough refrigeration space should be available at home to store the HPN solutions. Families should have access to a phone and should be given a phone number where a physician or a nurse can be reached round the clock in case of emergencies such as fever, catheter damage, catheter occlusion or other medical conditions requiring immediate care. For pump or solution related problems, the HPN provider company should be accessible by phone 24 hours a day.

All discharged HPN patients should be seen within a week by their physician to evaluate the programme and address problems experienced by the family. Careful serial weight and height measurements, done at each visit, give the best clue to the adequacy of nutrition. Serial weight measurement is more valuable for assessing short-term nutritional status. Children on HPN should also have developmental assessment done during each clinic visit. Both over and undernutrition should be avoided. In case of growth failure on presumed adequate parenteral support, nutritional reassessment including indirect calorimetry is indicated. Serum prealbumin level is an excellent indicator of short-term nutritional status. Prealbumin, measured at 4 days’ interval, indicates whether the subject is in an anabolic or catabolic state. However, it must be realized that a low prealbumin level may result from an inadequate protein intake as well as from insufficient energy supply. Attempts should always be made to maximize use of oral/enteral feeds to the level of tolerance of the patient. Parenteral support should be reduced if the patient shows excessive weight gain. Electrolytes should be remeasured during each clinic visit and adjustments made in the solutions for parenteral nutrition if required. Liver function tests should be done quarterly on a stable patient. Trace elements such as selenium, manganese, zinc, copper and chromium should be monitored annually. Infants and children need close follow-up. Infants should be seen in the clinic weekly for a month after discharge, every two weeks till 6 months of age and then monthly till the first birthday. Children, depending on age and clinical condition, can be followed up at intervals of one to three months.
The importance of initiating oral or enteral feeding cannot be overemphasized. Even in children who cannot absorb any nutrients enterally, oral and/or enteral feeding should be encouraged. When the subject tolerates significant amount of enteral feeds, we attempt to gradually decrease parenteral support. Initially either the HPN infusion is stopped for one day a week or the daily infusion is decreased by 10%. The child’s weight and intestinal output should be followed daily to weekly while decreasing parenteral support. It is not unusual for the child to lose weight immediately after parenteral nutrition withdrawal which he/she gradually gains back.

Complications of long-term HPN

Long-term HPN limits the patient’s and the family’s freedom to some extent. With modern techniques most of these limitations can be overcome. Vacations for the patient and the family can be planned. We have had families with their children travel to Europe, Asia and throughout North America safely and successfully. It takes planning but can easily be accomplished. As these children receive a large amount of fluid at night, frequent urination can disturb sleep and enuresis may be a problem especially in male children.

CVC infection and sepsis

Sepsis is the most serious and frequent complication in infants and children on HPN. Over the years we have seen a significant reduction in the HPN associated infections in children and adults. Most of our patients are infection free for prolonged periods of time while a few have recurrent infections. Overall, children had a sepsis rate of 0.37 per patient-year on HPN in our programme [27]. We have had substantial numbers of patients infection free for 5, 10, 15 and 18 years on HPN. This seems to be due to the quality of the caretaker and their fastidiousness in following our protocol. Any fever in a patient on HPN should be suspected as sepsis unless an obvious source such as otitis media is found. Fever occurring during HPN infusion and/or accompanied by chills are highly suggestive of line infection. A detailed history should be taken regarding possible breaks in HPN protocol which are the commonest causes of line sepsis. The line itself, the entry site and the tunnel should be examined. All children on HPN with significant fever should have bacterial (aerobic and anaerobic) and fungal blood cultures drawn from the line, in case of double lumen catheter one set from each port; a haemogram with differential count and urine analysis should also be done.

We err on the side of treating and routinely administer two antibiotics (vancomycin for Staphylococcus and coverage for Gram-negative bacteria) through the CVC in all children with unexplained fever. In children with double lumen catheters, antibiotics should be alternated through each lumen. If cultures are negative but the patient is still febrile, other causes of fever should be investigated. Once the organism is identified, the antibiotics can be changed according to the sensitivity pattern. The catheter may have to be removed if the patient does not show improvement on appropriate antibiotic therapy. Gram-negative line infections, though less common than Gram-positives, are more difficult to treat. Forty-four percent (44%) of the CVCs infected with Gram-negative bacteria required removal of the line [27]. Fungal line infections, most commonly Candida, warrant immediate removal of the line. Patients are discharged home on antibiotics when clinically stable and afebrile for 24 hours.

The least number of antibiotics (ideally one; in complicated infection, two) on an 8 or 12 hourly dosage schedule should be prescribed for home use.

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* No unequivocal evidence of effectiveness
antibiotic therapy. Parents should be trained in infusing antibiotics prior to discharge. The duration of home antibiotic treatment is 2 weeks but may be extended to 4 weeks for complicated recurrent infections. Recently “antibiotic lock” has been used in line infections with known organisms and sensitivity [28].

The techniques of prevention of catheter infection mentioned at different places in this article are summarized in table II. Prevention, a high index of suspicion and early intervention are the keys to success with this dangerous complication of HPN.

Catheter occlusion

CVCs can be occluded by thrombus, fibrin deposition, calcium salt deposition, kinking of the catheter or if the catheter tip impinges on the venous wall. One of the earliest signs is withdrawal occlusion or failure to draw blood through the catheter. Thrombosis is a complication seen in both long- and short-term catheter use [29, 30]. Thrombus may form around the catheter, at the tip or within the venous lumen. Volume depletion, sluggish venous circulation, infection or hypercoagulable states predispose the patient to thrombus formation. Infected thrombi may act as a source of septic microemboli. Some patients may develop superior vena caval syndrome, though this is rare in children. Heparin and oral anticoagulants are used to prevent further thrombosis. Some studies suggest that long-term low dose oral anticoagulant may be helpful in reducing catheter thrombosis [31].

Catheter lumen patency, when not in use, is maintained by heparin flushes in Broviac and Hickman catheters. We use a flush of 3 ml of 100 units/ml heparin. Urokinase (2,500 IU/ml) is used to lyse the clot in a partially occluded catheter [32]. One to two ml of urokinase is put into the catheter and is capped off for 30-60 minutes or more if required. The urokinase is then aspirated and the catheter is flushed with heparin. A completely occluded catheter has to be removed. We have successfully used a low dose 24 hours urokinase infusion technique for clogged catheters unresponsiveness [33].

Mechanical damage

The catheter can break or develop a leak due to accidents or repeated clamping. This should be treated as an emergency. The risk of line infection is great in this situation. Occasionally the patient may bleed from the broken catheter. The catheter should be repaired under sterile conditions by an experienced nurse or physician with a catheter specific repair kit available from the manufacturer. If the damage is very close to the exit site, repair may not be possible and the CVC may have to be sacrificed. Catheters do wear out with usage and secondary to cleaning. However we have repaired and spliced some catheters as many as half-a-dozen times. One patient has had the same catheter for more than 14 years.

Liver and biliary system disease

Cholelithiasis or biliary sludge has been documented in 10% of all children on HPN, a significantly higher incidence than is found in the general paediatric population at autopsy (1 in 15,000). The biliary stasis and imbalances in chemical composition of bile thought to be responsible for this condition can possibly be reduced by enteral feeding. Children with gallstones need cholecystectomy. When long-term HPN patients undergo laparotomy for other reasons, prophylactic cholecystectomy should also be considered. Role of choleretic agents in this condition is not yet well established.

Serious life threatening liver disease is not common in our patient population on HPN. In a recent review we found that only 2 out of 26 (7.6%) children who were on long-term HPN in our programme, had progressive liver disease. Both patients had hepatitis C infection [34]. About two thirds of these children had past history of persistent rise of transaminases without clinically significant liver disease. Some of these patients have had other causes such as viral hepatitis or a history of ischaemic injury to explain the chronic liver dysfunction. Recent use of specially formulated infant amino acid solutions as well as emphasis on early and continued enteral feeding may be responsible for the decreased incidence of chronic liver disease in HPN patients [35].
Fluid and electrolytes

Asymptomatic hypokalaemia is the commonest electrolyte abnormality in HPN patients. Electrolytes, checked during clinic visits or obtained through the home care agency, can be used to customize electrolytes in the HPN solution. Fluid balance should be assessed during clinic visit. Additional supplemental fluids may need to be provided if the child has increased intestinal loss from an ostomy or diarrhoea. This fluid can be given concurrently with HPN or at the end of HPN infusion.

Iron, trace elements and vitamins

Modern HPN provides trace elements such as zinc, copper, selenium and chromium [36]. Recently there has been a concern about trace element overload. We do not use commercial multi-trace element formulations which may be responsible for chromium overload documented in children on HPN [37, 38]. We add individual trace elements to the HPN solution to avoid this problem. We have observed elevated manganese levels in HPN patients though we do not supplement manganese. Regular iron supplementation can lead to iron overload [39]. Patients need to have iron levels monitored at least every 6 months if iron is given routinely. Iron should be deleted from TPN solutions if iron saturation of binding capacity exceeds 50%. Despite usual supplementation, children with massive intestinal fluid loss may develop zinc and selenium deficiency. Early or mild zinc deficiency is characterized by loss of hair including eyebrows and eyelashes. Photophobia, a yellow crusting eruption around the mouth, nose and ears, as well as bullous eruptions at the base of the fingers, toes, anus and the genitalia are features of moderate or severe zinc deficiency [40]. Selenium deficiency has recently been recognized in children; it is characterized by decrease in hair or skin pigmentation, macrocytosis and loss of muscle strength [41]. Cardiomyopathy is described in adults but not in children with selenium deficiency [41-44]. The role of fluoride, manganese and cobalt supplementation are not yet well established; concerns about overloading remains.

Bone and renal disease

Most HPN patients develop an osteopenic bone disease of yet unclear etiology [46, 47]. Pathological fractures are rare. It can cause significant morbidity but mostly in adults. Deficiencies of fluoride, boron or silicon can be contributory factors but no definite preventive or therapeutic measures are currently available. Aluminium induced TPN bone disease should not be an issue if balanced amino acids and aluminium free minerals are used to manufacture TPN solutions. Vitamin D should be administered as part of the multi-vitamin infusion received daily.

Patients on HPN have shown a decreased glomerular filtration rate correlating with the duration of HPN. The clinical significance of this finding is still uncertain [48].

Growth retardation

Most of the children grow according to their growth potentials on HPN. Growth retardation, seen in a few, may be related to the patient’s underlying condition or may signify a genetically determined low growth potential [49]. There may be rare individuals who require unique nutrients for growth which are not well recognized. Alpha-ketoglutarate may be such a substance.

Development and social problems

A combination of factors like chronic illness, recurrent hospitalization, technical dependency and overprotection by parents can impair development in children on HPN. Prolonged hospitalization causes developmental delay [50]. This can be avoided by discharging the HPN patients from the hospital as soon as possible. In our patient popula-
tion, children on HPN have demonstrated a normal or nearly normal intelligence and motor functions when evaluated by standard age specific developmental tests [51]. The majority of the older children on prolonged HPN have mild perceptual motor deficits. However, most attend regular schools and participate in normal age related activities. Two of our patients on HPN for more than 17 years have entered college and are doing well. All adults in our programme who started on HPN in their adolescent or teenage years finished high school. Some went to college and all are gainfully employed. None have married.

**Duration of HPN, mortality and cost**

Over 230 children have been in our HPN programme during the past 22 years. Most have been able to discontinue it. Children can be on HPN for a few months to years. At present, among 33 subjects who were started on HPN since infancy, 5 are on HPN for more than 5 years, 11 for more than 10 years and 2 are on HPN support for more than 18 years.

The principle cause of death from HPN is catheter related sepsis which is largely preventable. Thirty-nine patients out of 230 have died in our HPN programme in the last 22 years. However, only 14 died due to HPN related complications. We have lost only one patient due to HPN related complication in the last 5 years. Nine patients died due to catheter sepsis and 3 from liver failure. Fluid and electrolyte imbalances and improper techniques can also be fatal but are entirely preventable.

Contrary to what many believe we rarely run out of access sites for catheters. We have had to perform only one thoracotomy to place a central catheter in a child during the 22 years of our program.

HPN is expensive but it is substantially less expensive than keeping a patient in the hospital for equivalent care. A typical child receiving HPN may have direct and indirect costs of $50,000 to $75,000 per year. In most states government financial support is provided if insurance does not cover the cost.

**References**