Learning Objectives

- Learn about the different types of central lines for parenteral nutrition;
- How to choose a venous access catheter for home parenteral nutrition (HPN);
- Insertion of central lines;
- Learn about the most common line complications.

Contents

1. Introduction
2. Choice of central line for HPN
   - 2.1. Venous access for short- and medium-term periods of parenteral support
   - 2.2. Venous access for long-term parenteral nutrition and HPN
      - 2.2.1. Tunnelled catheters
      - 2.2.2. Implantable ports
   - 2.3. Choice of central vein and insertion procedures
   - 2.4. Position of the distal tip of the catheter
   - 2.5. Loss of vascular access
3. Catheter related infections
   - 3.1. Introduction and definitions
   - 3.2. CRBSI, diagnosis and treatment
   - 3.3. Repeated line infections
   - 3.4. When to remove the line
   - 3.5. CRBSI, how to reduce the risk?
4. Catheter related venous thrombosis
5. Summary
6. References

Key Messages

- Chose venous access route and device in accordance with the needs of the patient;
- General use of antiseptic/aseptic techniques is of paramount importance in preventing infections;
- Support patient education in HPN procedures to minimise line-related complications;
- Adhere to ESPEN guidelines to manage complications;
- Support clinical studies of venous access for HPN patients.
1. Introduction

Intestinal failure is defined as a condition with reduced intestinal absorption to the extent that parenteral supply of macronutrients and/or water and electrolytes are needed to maintain health and growth. The condition may be transient if gut function can be restored, but home parenteral nutrition (HPN) is indicated for patients with chronic intestinal failure. The most common causes of intestinal failure are resection of the small bowel due to inflammatory bowel disease, a catastrophic event such as mesenteric thrombosis, other small intestinal disorders that cause malabsorption, and conditions with pseudo-obstruction. Also, patients with cancer and intestinal complications or cancer patients with a need of nutritional support may require HPN. The prevalence of HPN is rising and recent data report prevalence being in the range 1 to 25 patients/million population in European countries. The prognosis for patients with benign disease is reasonably good with a 5-year survival of about 75% (1-5). In contrast, the prognosis for the increasing number of patients entering an HPN programme with a malignant disease is poor (6). Overall, the number of HPN patients is low and referral to specialist centres should be considered, but this may not always be possible.

HPN requires a well functioning central venous line, but insertion and the use of lines are associated with complications. Some of these are serious for the patient, requiring admission to hospital, and furthermore increase the cost of the treatment. This LLL manuscript will focus on venous access and the most frequent related complications.

2. Choice of Central Line for HPN

When considering which type of venous device to use for providing parenteral nutrition a number of issues must be taken into consideration. These include the length of the period of treatment: short-term during a hospital stay, mid-term with continuing treatment after discharge from the hospital, or long-term for those with irreversible intestinal failure? The number of weekly infusions is also important for the choice of catheter. Patients with a previous history of complications related to vascular access may present a particular challenge and this must be taken into consideration. Also, the patient’s preference is important, and must address what is most practical for him or her and how a specific choice will affect body image. So the decision regarding venous access is best made by the patient in collaboration with an experienced HPN team (7).

2.1 Venous Access for Short- and Medium-term Periods of Parenteral Support

For treatment periods of up to 3 months, for patients staying in hospital or supported in a non-hospital but medical setting, choose a non-tunnelled polyurethane (PUR) catheter inserted into a central vein (subclavian, internal jugular). Catheters may have single or multiple lumens and are designed for continuous use (7, 8).

Medium-term catheters are also non-tunnelled and centrally located, but are intended for discontinuous use. In addition to PUR and silicone catheters (Hohn type), PICCs (peripherally inserted central catheters) may be used. All of these can also be used for up to 3 months in outpatients, but self-care is difficult with PICC-lines since the exit position from a peripheral vein of the arm often disables one hand. The rate of infectious complications with PICC line is reported to be lower in some studies and higher in others (9, 10) and the cost compared to ports and conventional central lines is lower (11). The risk of venous thrombosis is considered higher for PICCs compared to other central lines. Over the last few years the use of tunnelled PICCs has entered clinical practice; a tunnel may prevent infections ascending, and if placed at the level of the upper arm this type of device may be used for long periods. Experience and data in HPN are scarce.
2.2 Venous Access for Long-term Treatment and HPN

Long-term treatment requires a cuffed tunnelled central catheter such as a Broviac, Hickman or Groshong or a totally implanted port.

2.2.1 Tunnelled Catheters

Catheterisation of the superior vena cava with a tunnelled silicon catheter is the technique most commonly used for long-term parenteral nutrition. The felt cuff of the catheter allows fixation as the subcutaneous tissue adheres to the cuff, which is typically placed about 2.5 cm from the exit site. Multiple lumen catheters cannot be recommended for long-term treatment as an increased number of access points theoretically increases the risk of infection. Groshong© catheters have a rounded tip with a pressure sensitive two-way valve at the intravascular end. The valve is closed when the catheter is not used and opens outwards during fluid infusion or bolus injection. The valve can open inwards and blood can be drawn, although this is not a recommended procedure. The advantages of all the tunnelled catheters are that they can be used for several years, connecting to infusions does not require the puncture of the skin (in contrast to implantable ports), and if the external part of the catheter is damaged, it can be replaced using a repair kit.

2.2.2 Implantable Ports

Another option for the administration of parenteral nutrition is the totally implantable port. A stainless steel chamber with a membrane is implanted in a subcutaneous pocket in the chest wall and its catheter part is placed in the subclavian vein with the tip in the superior vena cava or right atrium. The advantage is that the skin covers the port, which is practically invisible, so no dressing is needed and the body image is unchanged and swimming will not increase the risk of line infection. Among the disadvantages is the need for perforating the skin for infusions. Compared to catheters with an external segment, ports generally require more frequent replacement. When infected, antibiotic treatment will generally not save a port, which then has to be removed surgically (12). Some studies indicate that infection rate is lower for ports, but these studies have mostly been carried out in patients receiving chemotherapy. The few comparisons between lines and ports for HPN do not indicate a lower infection rate for ports (13). So the choice between a tunnelled device and a port depends on several factors, patient preference, the frequency of use of the VAD and the skills of the staff involved.

Key points: which type of venous access for HPN

- PICCs only for in-patients and not recommended for HPN;
- Broviac or Hickman or similar for long term use and for patients needing daily access;
- Implantable ports can be used, advantages regarding the body image;
- Choices to be made by the patient in collaboration with the HPN team.

2.3 Choice of Central Vein and Insertion Procedures

Studies carried out in the intensive care setting indicate that subclavian puncture is associated with a lower frequency of catheter related infections than jugular insertion (14); confirmatory data specific to HPN are currently missing. A key advantage of subclavian cannulation for HPN is that the exit site of the tunnelled catheter can be placed to allow the patient self-management of parenteral nutrition and this is obviously important. Access on the right side of the body is recommended due to a lower risk of thrombotic events, although this is not strongly supported by data. There is solid evidence that the use of ultrasound guided venous puncture reduces the incidence of complications and provides a higher success rate compared to access obtained without using imaging (15). Among the potentially avoidable complications in relation to insertion are arterial puncture, pneumothorax and damage to neck structures.
2.4 Position of the Distal Tip of the Catheter

Long term parenteral nutrition with its high osmolality requires central venous access and should therefore be infused in the lower third of the superior vena cava or at the junction of the right atrium. Thus after insertion it is strongly recommended that the position of the tip is verified using x-ray or fluoroscopy. In a retrospective study of 141 central venous lines, the location of the catheter tip was the only factor found to be statistically predictive of malfunction (16). A significant increase in malfunction was observed in cases where the catheter tip was located more than 4 cm superior to the junction of the right atrium and the superior vena cava. Malfunctions were least likely in those cases where the catheter tip was located in the right atrium. Also, the risk of thrombosis is considered less if the tip of the catheter is placed as indicated above (17). The position of the distal tip of the central venous catheter is important for increasing its longevity and minimizing adverse events in patients on HPN.

2.5. Loss of Vascular Access

Patients on HPN for many years may encounter repeated line complications with venous thrombosis, and loss of vascular access may eventually be the result. When the 4 key neck veins (subclavian and internal jugular) have been lost or if there is a central venous thrombosis, it will be necessary to consider use of the femoral veins, but the risk of infective complications is higher (14, 15, 18), and the practicalities of access may also pose problems. Case reports of access by direct puncture of the right atrium or by cannulation of the hepatic veins have been reported (19), as have occasional uses of the azygos and other smaller veins. The use of an external arterio-venous graft for intravenous nutritional support may also be an unconventional option that has proved successful (20). There is an evolving interest in endovascular re-canalisation of thrombosed veins, but this remains experimental and limited to specialist centres. It is important to consider the possibility of intestinal transplantation when venous access is compromised. Referral for evaluation of transplantation should not wait until only a single vascular access route remains open, since the haemodynamic and nutritional demands of the patient during the peri-operative period may demand greater access if a transplant is performed (7).

Key points: Catheter insertion and position
- Sterile conditions when inserting catheters to reduce infectious complications;
- Lower rate of complications with subclavian < jugular < femoral veins;
- Ultrasound to guide when inserting;
- Avoid using femoral veins due to higher risk of complications;
- Catheter tip at junction of vena cava and atrium results in fewer malfunctions;
- If venous access is seriously compromised consider referring for intestinal transplantation.

3. Catheter Related Infections

3.1 Introduction and Definitions

Infectious complications are the most serious problem related to vascular access devices. For patients on HPN infections add significantly to morbidity and mortality (21). The pathogenesis is bacterial or fungal growth, initially colonising the catheter, both the luminal and the outer surface, and this may spread and give rise to a catheter related blood-stream infection (CRBSI) if the pathogens reach the blood-stream. Contaminations of the hub, a broken line or the use of the catheter for non-nutritional purposes are probably the most common endoluminal causes of infection. Micro-organisms migrating along the catheter from the skin or introduced during its insertion cause infection of extraluminal origin.
The catheter infection rate reported from various HPN centres is in the range 0.3-0.5 episodes per patient year (22,23). Some centres report higher infection rates. Catheter colonization is defined as growth of more than 15 colony-forming units per $\mu$l at semi-quantitative culture or more than $10^3$ colony-forming units per $\mu$l (quantitative culture) from a proximal or distal catheter segment in the absence of accompanying clinical symptoms (24). Exit-site infection involves erythema, tenderness, induration or purulence of the skin within 2 cm of the exit site of the catheter. Pocket infection is defined from erythema and necrosis of the skin over the reservoir of a totally implantable device, or purulent exudates in the subcutaneous pocket containing the catheter and extending more than 2 cm from the exit site or the pocket of an implantable device. Catheter related bloodstream infection is defined by the isolation of the same organism (identical species and antibiograms) from cultures from catheter segments and blood cultures from a peripheral vein, in a patient with clinical symptoms of blood stream infection and no other apparent source of infection. Probable systemic catheter related sepsis is characterised by a colonized catheter associated with clinical signs suggesting septicaemia, despite the lack of positive peripheral blood culture.

3.2 CRBSI Diagnosis and Treatment

From a clinical point of view it is important to recognize both the local and the systemic manifestations of a catheter related infection. The local sign of infection at the exit site of a tunneled catheter is easily recognised and include redness of the skin, local pain, or discharge of pus from the tunnel, which may appear elevated due to the inflammation. In contrast, the systemic features cover a broad range of symptoms, but typically the patient will complain of fever and chills that may appear immediately or hours after the infusion of parenteral nutrition is commenced. However, the symptoms can be very non-specific and patients on HPN who present with new complaints should always be suspected to have CRBSI. Some of the non-specific features that may appear include those of cardiopulmonary origin such as dyspnoea and arrhythmias, and a variety of gastrointestinal complaints. Once a catheter associated infection is suspected blood cultures should be taken to diagnose a possible bacteraemia, and systemic antibiotic treatment is generally recommended whilst awaiting the results of the cultures. Cultures of blood from both central and peripheral sites should be evaluated, since it is difficult to determine whether a positive culture of blood from a central line indicates contamination of the hub, colonisation of the catheter or catheter related bloodstream infection. The longevity of lines should be kept as high as possible since repeated insertion of new lines carries a risk of complications and a cumulative loss of vascular access. Antibiotic lock therapy for 2 weeks is supported by a clinical study and is recommended (25). However, if the patient has clinical signs of septic shock the catheter should be removed immediately.

3.3 Repeated Line Infections

If patients on long-term HPN encounter repeated line infections, intervention apart from changing the line may be appropriate. Re-education in all necessary procedures should be carried out in all patients with line sepsis. Other measures that have been applied are the use of line locks with antibiotics, urokinase to lyse thrombus, and possibly alcohol and/or strong acid to dissolve debris (26), but no controlled studies of such interventions in HPN are available. Lock procedures may be used to prevent repeated infections, and a recent study using taurolidine, an antiseptic with broad antimicrobiological activity has successfully been used in a single controlled study using a cross-over design in HPN patients (27). We are awaiting the results of ongoing controlled studies with lock procedures using taurolidine.
3.4 Removal of the Line

The tunnelled line or port is removed in case of tunnel infection, port abscess, clinical signs of septic shock and if the microbiological diagnosis is a fungal infection. Complications related to the infection, endocarditis or other metastatic infections as well as thrombosis will also dictate line removal. Otherwise efforts should be made to try to save the line using all the standard procedures. Generally, treatment with relevant antibiotics should continue for at least 10 days. If the line is removed the insertion of a new device should be postponed until a few days after finishing treatment with antibiotics.

3.5 CRBSI – Reducing the Risk

Tunnelled catheters and implanted ports are specifically designed to protect the patient from extraluminal contamination and should be used for all patients who need parenteral support for periods exceeding 3 months. Significant reductions in infection rates have been reported with coated central lines (antibiotics and metals), but such devices are only intended for short-term use. Unless more lumens are required for patient management the single lumen catheters should be preferred as controlled studies show that they reduce infection risk. Avoid the placement of catheters in the femoral vein since this route is associated with more complications including thrombosis and infection (18). The proper and full education of patients and caregivers are of paramount importance in reducing the risks of infection. This is supported by clinical studies in HPN patients (28). Central lines should not be changed routinely; there are no data demonstrating that this will reduce the risk of infection. A number of agents including antibiotics, alcohol and citrate, have been used for flushing the line to reduce intraluminal biofilm formation, but evidence of useful effects in HPN is lacking. Taurolidine may be an exception (27), but we await more studies before advocating its use in general or in high risk patients. The use of heparin for flushing does not reduce the risk of infection.

4. Catheter Related Venous Thrombosis

Catheter related venous thrombosis (CRVT) is a severe complication that may result in the loss of central venous accesses in HPN patients and may be an indication for intestinal transplantation if it affects two or more of the central venous vessels. A thrombosis may be clinically manifest or subclinical and can develop soon after catheter insertion or be delayed and appear in patients with long-term catheterization. Most of the data on the incidence of CRVT in HPN comes from retrospective series (23) with large patient cohorts that reported only on clinically manifest thrombosis. In these studies, the incidence is in the range 0.02-0.09 cases/catheter/yr or 0.12/1000 catheter-days. In a recent prospective study of the HAN&CIF group in 62 patients on HPN, the incidence of CRVT with serial Colour Doppler Duplex Sonography (CDDS) evaluations for 12 months after catheter insertion was 0.045/catheter/year, quite similar to that found in retrospective studies (29). In this study, all the catheters were inserted with ultrasound guidance or radiologic control and the catheter tip was located in the atrio-caval junction or in the lower third of the superior vena cava in all subjects. The pathogenesis is probably multifactorial and includes vessel injury during insertion of the catheter, stasis due to the indwelling device, damage to the endothelium caused by high osmolality infusions, and catheter-related infections. It is more common when the catheter tip lies high in the superior vena cava. The primary feature suggesting a thrombotic event is usually malfunction of the catheter. Swelling of the arm and neck and prominence of the superficial veins of the chest may ensue. There is a risk of pulmonary embolism. The diagnosis relies on the clinical picture and can be confirmed...
by (CT) angiography and sometimes by Doppler ultrasound scans. If not functioning properly or if associated with infection the catheter should be removed. Anti-coagulant treatment should be initiated and most centres will continue with a vitamin K antagonist (such as warfarin) for as long as the patient has a central line, but no studies in HPN patients are available. The role of new oral anticoagulants (direct factor Xa inhibitors or direct thrombin inhibitors) in the treatment may be promising as they need little monitoring (30). In patients whose underlying disease is benign a more aggressive approach with systemic thrombolysis and thrombectomy may be considered. Also, stenting procedures may be used in the experienced setting.

Prevention is most important and includes careful selection of the insertion site and adjustment of the position of the tip of the catheter to ensure it lies at the junction of the superior vena cava and the right atrium.

Key points: Catheter related infection and thrombosis

- Central venous catheter-related infections should be managed according to current guidelines on long-term intravascular catheters;
- A conservative approach with systemic and local (locks) use of antibiotics is recommended for simple infections;
- Catheter removal is first line action in case of infections with fungi, highly virulent bacteria or septic complications;
- Repeated line infections may be reduced by antibiotic lock procedures;
- Thrombosis related to the catheter is a relatively rare but serious complication. Patients should be treated with anti-coagulants;
- General barrier precautions and education of patients is of paramount importance for prevention of infectious complications.

5. Summary

Broviac or Hickman tunnelled lines are recommended for long term use and for patients needing daily access. Implantable ports can be used with advantage regarding the body image, but PICCs are only recommended for in-patients. Catheters should be inserted under full sterile conditions to reduce infectious complications. There is a lower rate of complications with subclavian than jugular veins and when ultrasound guidance is used. The safest site for the catheter tip is just beyond the junction of the superior vena cava and the right atrium; use of the femoral veins is not recommended due to a higher risk of complications. Thrombosis related to the catheter is a relatively rare and serious complication that can result in loss of venous access. If venous access is seriously compromised referral for intestinal transplantation should be considered. General aseptic barrier precautions and education of patients is of paramount importance in reducing the incidence of catheter related infections and other complications. Non-serious catheter related infections should be treated with antibiotics and lock procedures aiming at saving the line. Infections with fungi and highly virulent bacteria require line replacement. Repeated line infections may be reduced by antibiotic/antiseptic lock.

Further suggested reading, ESPEN guidelines, kindly look up the website.
6. References


