Practical aspects of peripheral parenteral nutrition

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Purpose of review
The purpose of this review is to provide an update on the advantages and disadvantages of using peripheral parenteral nutrition, including the techniques, indications and results.
Recent findings
The new catheters, together with a better knowledge of intermediate metabolism, permit the use of peripheral parenteral nutrition in many clinical situations during short periods of time.
Summary
Peripheral parenteral nutrition is an alternative to total parenteral nutrition, and is a complement to enteral nutrition and the oral route. Progress in catheter design and materials, infusion techniques and an improved knowledge of the optimal nutriments has made peripheral parenteral nutrition a safe, efficient and useful method to treat patients over certain periods of time.

Keywords
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Abbreviation
TPN total parenteral nutrition

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Introduction

The need for central vein catheters for the administration of total parenteral nutrition (TPN) has been an important inconvenience and a source of frequent mechanical and septic complications. The possibility of administering parenteral nutrition through a peripheral route has been an important target. However, the high osmolarity of parenteral nutrition solutions limits its tolerance through the peripheral route, and the large volume of solutions to be infused in order to maintain acceptable osmolarity limits the amount of nutriments that can be administered. Progress in catheter design and materials, infusion techniques and an improved knowledge of the optimal nutriments has made peripheral parenteral nutrition (PPN) a safe, efficient and useful method to treat patients over certain periods of time.

A review of 1261 patients receiving artificial nutrition conducted by the Spanish Society of Intensive Medicine [1] showed that 18.2% of patients were receiving PPN, whereas 38.5% received TPN, and the rest (53.3%) received enteral nutrition. Similar data have been reported by Anderson *et al.* [2••].

Although the American Society of Parenteral and Enteral Nutrition Guidelines of 2002 [3••] stated that PPN is not the optimal choice for feeding patients with significant malnutrition, because of severe metabolic stress, large nutrient or electrolyte needs, fluid restriction or the need for prolonged intravenous nutritional support, and that such patients should be nourished through a central vein, some of them may also be fed, at least partly and for short periods of time, through the peripheral route.

Definition of peripheral parenteral nutrition

PPN is the kind of artificial nutrition capable of being administered through an accessible subcutaneous vein. TPN administered through a long catheter, inserted through a peripheral vein but with the tip located in a high flux central vein, is not considered to be PPN.

The concept of PPN sometimes implicitly carries the idea of hypocaloric nutrition due to the fact that in most cases volume or osmolarity limitations force the administration of amounts of energy and nutriments that do not meet 100% of the patient's needs. However, in patients who tolerate or need large quantities of fluids, PPN may meet all energy and nutrient requirements.

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Targets

A negative nitrogen balance is synonymous with fat free body mass loss, reduction of body cell mass and beginning of functional alterations related with malnutrition. The aim of PPN is to minimize negative nitrogen balance in patients unable to meet their nutritional requirements through the gastrointestinal tract, either because of difficulties in oral or enteral nutrition or by an increase in metabolic demands due to stress situations, secondary to the disease.

Although PPN may, in some instances, cover all nutritional requirements, this target is not met in many circumstances. PPN should be considered a temporary method to nourish patients while oral or enteral nutrition is resumed. PPN is an excellent way to minimize the cumulative effect of a negative nitrogen balance secondary to periods of starvation, very frequent in our hospitalized patients. PPN may also be a complementary therapy for patients tolerating limited quantities of nutrition through the oral or enteral route. In this way, a 'combined artificial nutrition' with enteral nutrition and PPN may meet all nutritional needs, obviating the neccessity for a central catheter. PPN has usually been recommended in patients considered to require nutritional support for periods under 7 days. Present trends have increased this figure to 14 days, as long as nutritional requirements are covered. This is important because most of the periods of TPN support used in hospitals last less than 14 days, and a quarter last less than 7 days [4]. For more prolonged periods of time, TPN should be prescribed.

Nutrient and volume needs

Minerals, vitamins and trace element needs are easily met with small volumes administered intravenously or intramuscularly in hospitalized patients. Electrolyte requirements (sodium, potassium, calcium, magnesium and phosphorus) might pose a greater difficulty but, taking into consideration that most patients require more than 2000 ml a day, these therapeutic objectives are easily met in the majority of cases.

The main problem lies in trying to cover protein and energy requirements that need large quantities of glucose or triglyceride emulsions. Although energy administration and a positive energy balance are mandatory in order to obtain a positive nitrogen balance, it is very difficult, and sometimes impossible, to achieve a positive nitrogen balance in some catabolic situations, even with the administration of very large quantities of energy, an action that, on the other hand, is associated with multiple deleterious effects [5], especially hyperglycemia [6].

The concept of hypernutrition has been abandoned, and we must accept our ignorance about the optimal energy support associated with the least number of complications, especially in view of the fact that some of the studies conducted with hypocaloric nutrition show a lower complication rate, at least during the first days of treatment [6,7•,8••,9•]. In this context, we must admit that it is not necessary to cover the total amount of basal requirements. Therefore the calorie : nitrogen ratio of 150 : 1 does not have to be reached.

Only a minority of hospitalized patients has a body mass index under 20; many are overweight. Therefore, most patients have enough body reserves to undergo several days of starvation. However, glycogen liver reserves last only a few hours and muscle glycogen can only be used by muscle, whereas other tissues, such as red cells, nervous system or kidney medulla cells, depend exclusively on glucose in order to produce energy. Therefore, fasting gluconeogenesis depends on body protein catabolism, and to a minimal extent upon glycerol released by triglycerides. In this situation glucose becomes an essential nutrient to stop protein catabolism.

This protein-sparing effect reaches its maximum with 150 g a day of glucose unless amino acids are simultaneously administered. Therefore, 150 g a day of glucose is the minimum amount that has to be administered in all patients under PPN. Additional quantities of glucose have a further nitrogen-sparing effect if administered simultaneously with amino acids, and this effect is shared with lipids when the minimum glucose requirements are covered. In this situation, the carbohydrate : lipid ratio may be approximately 50 : 50. Lipid administration is, in any case, an additional source of energy contributing to protein conservation, diminishing PPN osmolarity and the risk of phlebitis.

Although amino acid requirements in the normal individual are 0.8 g/kg a day, in most patients under metabolic stress it is preferable to administer 1–1.2 g/kg a day. Additional quantities might be beneficial in severe metabolic stress, but may be limited by the osmolarity of the solution. Therefore, it may be considered that adequate amino acid quantities range between 1–1.2 g/kg a day and glucose 150 g a day.

Volume limitation

Although elderly patients and patients with renal, hepatic, cardiac disease or in situations associated with inadequate antidiuretic hormone (ADH) secretion may have difficulty in handling volumes greater than 2000–2500 ml a day, most adults tolerate well volumes up to 3500 ml a day. Clinical situations with a large volume loss, such as high output fistulae, profuse gastric aspirates, polyuria, etc. condition increased water needs that can be used as a vehicle for additional nutrient administration.

Although the tolerance of peripheral veins reaches 600–900 mOsm/l, depending on other factors, such as the pH and the presence of lipids, osmolarity must be limited to 600 mOsm/l. Therefore, the volume must range between 2500 and 3500 ml in order to reduce osmolarity and to maintain an adequate fluid balance according to the patient's needs and tolerance. High output fistulae, considered by some as a contraindication for PPN, can in some instances be managed with PPN.

PPN solutions can be manufactured in the hospital pharmacy as any other artificial nutrition solutions. Alternatively, ready-to-use 'all in one' solutions can be used, although in some instances they cannot be adapted to the patient's needs (Table 1).

Thrombophlebitis and peripheral parenteral nutrition

The use of PPN poses two problems: the difficulty of assuring an adequate amount of calories to cover the needs of each patient, and the risk of phlebitis. The latter is not only a source of discomfort for the patient, but it forces the rotation of venous access, which becomes a great obstacle when venous access is difficult. The incidence of phlebitis varies between 2.3 and 70% [2••,10,11•]. These marked oscillations are caused by the criteria used to diagnose them.

The origin of thrombophlebitis in these patients is multifactorial (Table 2). One of the most important factors is the nature of the solution to be infused. Both osmolarity and pH have a clear influence. Therefore, the solutions to be infused must have an osmolality between 600 and 900 mOsm within a pH range of 7.2–7.4, although osmolarities as high as 1200 mOsm have been well tolerated when heparin–hydrocortisone has been added to the parenteral nutrition solution, and patches of nitroglycerin are placed close to the point of infusion [10,12].

The catheter material is also important. With polyurethane catheters the incidence of phlebitis is reduced by 36%. Silicone elastomer catheters are also quite safe, but the former have the advantage of a higher internal gauge with the same external diameter. Thick catheters have a higher incidence of phlebitis, as well as infusions that last for long periods of time [10]. Other factors are the catheter placement site, with a greater incidence in veins located in flexures, or the size of cannulated veins, with a higher incidence of phlebitis in smaller veins. A factor known to elevate the incidence of phlebitis is the presence of particles in the solution. For this reason, some authors recommend the use of filters in infusion lines. Bacterial colonization seems to be another cause, but the presence of skin saprophytic bacteria in the catheter tip when removed does not seem to be a relevant factor [2••,12].

It is important to establish a strict protocol of management of peripheral veins in order to reduce the incidence of thrombophlebitis. There are a few measures that have been shown to be important (Table 2). The addition of buffer solutions such as bicarbonate 1% seem to reduce the incidence of phlebitis. The high osmolarity of solutions containing glucose can be reduced partly by adding lipids as an alternative source of calories. Energy requirements would be covered, whereas osmolarity and, in turn, the incidence of phlebitis would be reduced. Glucocorticoids and heparin have also been used to reduce phlebitis. Heparin has the disadvantage that it promotes instability in all-in-one solutions by forming calcium–heparin–lipid complexes, but this issue has been questioned. Topical measures are of interest because of their easy application and lack of adverse effects. Transdermic trinitrate glycerine patches at the site of infusion increase blood flow and may contribute to a decreased frequency of phlebitis [2••,13].

Conclusion

The addition of lipids to parenteral nutrition solutions ensures an adequate content of calories with an outstanding reduction in osmolarity. This allows the use of peripheral veins for complete solutions, notably reducing the complications of classic TPN. Another additional advantage is a reduction and simplification of work for nurses and physicians in charge and the lowering of costs. Easy preparation procedures for PPN solutions and the availability of all-in-one solutions make them very safe from a point of view of sterility and stability, allowing immediate nutritional support once it has been indicated. Most of the patients requiring nutritional support will need it for periods shorter than 10–14 days. In these patients, PPN offers adequate nutritional guarantees with the above-mentioned advantages.

If the ultimate goal of any nutritional support is its efficacy, and this can be achieved with PPN, we must concentrate our efforts in counteracting the frequency and severity of its most important complication: peripheral thrombophlebitis. In most occasions PPN will be administered satisfactorily following certain protocols. Catheter placement must be performed under strict control. Catheters must be thin, preferably made of polyurethane or silicone elastomers and placed in a vein of an adequate size. Nitrites or topical anti-inflammatory drugs may be of use in the prevention of complications, but the moment these appear they will be useless and a change of location of the catheter must be recommended. The most effective measure in preventing

Table 1. Composition of different peripheral parenteral nutrition solutions

Product	Company	Volume	Aminoacids (g)	Glucose (g)	Lipids (g)	Na (mmol)	K (mmol)	Cl (mmol)	Ca (mmol)	P (mmol)	Mg (mmol)	Zn (mmol)	Energy (Kcal)	Osmolarity (mOsm/l)
Nutriflex Lipid peri	Bbraun	2500	80	160	100	100	60	96	6		6	0,06	1910	840
Nutriflex Lipid Basal	Bbraun	2500	64	250	100	100	70	80	8	30	8	0,06	2210	995
OliClinomel N4-549	Baxter	2500	56,25	200	50	53	40	50	5	21	5,5	–	1525	750
Clinimix N9G15E	Baxter	2000	55	150	–	70	60	80	4,5	30	5	–	820	845
Clinimix N9G20E	Baxter	2000	55	200	–	70	60	80	4,5	30	5	–	1020	980
Kabimix 1800	Pharmacia	2580	57	150	100	80	60	80	5	28	5	–	1830	695

Table 2. Associated factors to the risk of thrombophlebitis and possible prophylactic measures

1. Possible etiological factors
   - Catheter size
   - Catheter material
   - Bacterial colonization of catheters
   - Infused drugs
   - Length of infusion
   - Nature of the solution infused (pH and osmolality)
   - Particles present in the infusion
   - Site of catheter placement
   - Trauma related to venopuncture
   - Vein size
2. Prophylactic measures against thrombophlebitis
   - Buffer solutions
   - Glycerol
   - Local nitrites (5 mg patch)
   - Sodium heparin (600 U/l of solution)
   - Hydrocortisone (6 mg/l of solution)
   - Lipids
   - Local antiinflammatory drugs
   - Nutrition support teams

complications is to reduce the osmolarity by adding lipids, and to avoid manipulation whenever possible by using all-in-one solutions.

When evaluating a patient it must be stated if he or she needs nutritional support. If the answer is positive, the enteral route is the first choice, always more physiological, with lower costs and almost without complications. If the enteral route is not feasible, the patient has a moderate stress situation and the expected length of nutritional support is less than 10–14 days, PPN will be the choice, if there is no central catheter implanted. A proof of efficacy and safety of PPN is that it is the first choice in newborns and children, and is capable of maintaining the nutritional situation and promoting growth even though the nutritional requirements of children are proportionally higher than adults. Hypercaloric nutrition, recommended in situations of stress, although questioned at present, must always be administered through a central vein.

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