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CONSIDERATIONS AND STRATEGIES DURING TOTAL PARENTERAL NUTRITION: STABILITY AND COMPATIBILITY IN TPN SOLUTIONS PREPARATION, COMPONENTS OF A TPN REGIMEN, RATE OF INFUSION AND RATE FLOW OF INTRAVENOUS FLUIDS, INDICATIONS, CONTRAINDICATIONS AND COMPLICATIONS

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ABSTRACT

Total Parenteral Nutrition [TPN] has become vital in all clinical units and nearly all departments, especially the surgical unit, in hospitals and nearly in most clinical settings and home care services. It provides the major patient nutritional needs via [IV] route and proved lifesaving in clinical settings, where eternal based therapy is not possible. Despite potential advantages, it has limitations such as being expensive, Patient's incompliance due to administration need clinical intervention and complications in prolong use especially in high concentration as in thrombosis and diabetes. Components include mainly water, electrolytes, glucose, amino acids, fats, and vitamins. Over the past decades it has been grown worldwide but unfortunately it is connected with significant mortality and morbidity. The purpose of this review is to describe considerations and strategies regarding calculation steps Of TPN Solution, components of a TPN regimen, rate of flow of intravenous fluids and rate of infusion, indications, complications, contraindications Stability and Compatibility in TPN Solutions Preparation during parenteral nutrition.

1. INTRODUCTION

Total parenteral nutrition [TPN] a method that bypasses the GIT system and deliver fluids via vein in order to provide the nutritional support of essential electrolytes and nutrients to patients in various critical heath conditions such as malnourished patients. Components included in TPN administration are mainly water, electrolytes, glucose, amino acids, fats, and vitamins. it can supply a best way to provide nutrition through oral, parenteral and enteral routes. For those patients in whom full nourishment through these routes is not a feasible option, TPN is a valuable therapy for sustaining life.

It supplies almost all of the patient daily nutritional requirements. A peripheral vein is used for a short term period but longer period of use with a concentrated solution can lead to thrombosis. Therefore, central venous access is required. TPN, is not only used in hospital but also a good way to provide big source of nutrition specially to those who have lost bowel function in order to lead a healthy life.

Basic TPN Solutions are prepared using a sterile techniques, in liter batches according to the standard formulas. They can be modified based on specialized patient's need and laboratory results and underlying disorder. Adequate calories are supplied along with sufficient protein to prevent malnutrition. Most calories are given as a carbohydrates, 4-5 mg/kg/min in the form of a dextrose solution related to the metabolic needs. Lipids emulsions added to supply further essential fatty acids and electrolytes can be used to meet patient needs. In addition to these components, vitamins, water and trace elements are also a part of this therapy.

2- BEGINNING OF TPN

During insertion of TPN line, strict sterile technique is selected. External tubing must be cleansed every 24 hours. Dressing must be kept sterile and changed adopting sterile techniques as catheter remains at a place for a long time. Patient is instructed to recognize the symptoms of infection if getting a therapy outside hospital. The solution is started slowly initially and

energy and nitrogen are given simultaneously. Progress must be followed by a flowchart. Complete blood count is obtained. Liver test must be timely done and plasma protein, urine osmolality, magnesium, calcium, phosphate is measured and any change in transthyretin reflects clinical status.



3-PATIENT SELECTION

The administration of parenteral nutrition should be considered whenever adequate nutrition is hardly maintained, through the gastrointestinal tract. In general, parenteral nutrition should not be initiated unless it is anticipated that intravenous support will be required for at least five days, although preliminary data indicate as 72 hours preoperatively may be beneficial for malnourished patients.

An exception to this restriction is in the treatment of malnourished or stressed patients for whom nutritional support is urgent but whose gastrointestinal function is questionable. With these and other selected patients it is advisable to begin parenteral and enteral nutritional support simultaneously. Concomitant infections elsewhere in the body, diabetes, and obesity are not in themselves contraindications to parenteral nutrition.

It is recognized that these conditions increase the risk of septic complication during parenteral nutrition, but, with proper care, the incidents of infectious complications should be only 4 to 5.

Percent, or less, with little morbidity. Patients with either demonstrate a marked hypermatabolic response as great as that seen with trauma or stress. Therefore, instead of being a contraindication to parenteral nutrition, infection is a relative indication.

- For patients with any renal insufficiency, reduced content of proteins.
- Limited liquid intake is required for kidney or heart failure.
- Emulsion containing lipid provide non- protein calories for respiratory failure.
- Low dextrose concentration needed for neonates.
- General indications required long term nutrition, more than 10 days due to serious GIT malfunctioning or inability for essential feeding. Specific indication required for those patients who cannot absorb nutrients or unable to eat well due to massive bowel resection, radiation enteritis, diarrhea along with certain others as under;
- Malnourishment due to dose chemotherapy or radiation therapy.
- Patient undergone bone marrow transplantation.
- Patient with nonfunctional GIT.
- Patient with necrotizing pancreatitis.
- Catabolic patients with close head surgery, trauma or burn.

4. COMPONENTS OF TPN

Mixture of TPN has a separate components containing dextrose, amino acids, electrolytes, lipid emulsions, trace elements and minerals, however main three are macronutrients containing;

1. LIPD EMULSION

They provide calories and essential fatty acids to prevent deficiency of many of them in 3 weeks, 25-30% of total calories.

2. PROTEINS

They are given as mixtures of essential and non-essential synthetic L-amino acids. The eight amino acids as cannot be synthesized by a body include are, arginine, glutame, choline, taurine, S-adenosyl-Lmethionine etc. The healthy adult required 0.8-1gm/kg/day. Critically ill patient requires 1.5gm/kg/day. The amount of nitrogen is necessary to establish positive balance using a factorial needs. The daily nitrogen input is observed until calculation shows appositive nitrogen balance. The amount of protein required depends on a clinical situation and degree of malnutrition. The value of protein is based on the metabolic state of the required nitrogen, as example: For the Basal the required is 0.15g/kg/25h, Catabolic is 0.2g/kg/h and for the hypercatabolic is 0.3g/kg/h.

Complications

Parenteral nutrition is expensive, complex and can be associated with life-threatening complication. Enteral nutrition has the advantage of being more physiological, less complicated compared to TPN. TPN provides the nutritional requirements such as electrolytes, minerals, vitamins and water etc. for patients who have lost small – bowel function to lead useful lives.

Indications for Total Parenteral Nutrition

1. Massive small bowel resection
2. Diseases of the small bowel
3. Radiation enteritis
4. Severe diarrhea
5. Intractable vomiting
6. Malnourished patients, who are undergoing high dose chemotherapy, or radiation therapy.
7. Patients who have undergone bone marrow transplantation Patients with severe malnutrition and nonfunctional gut.

Components of a TPN regimen

A 70 kg human is composed of approximately 55% water, 40% organic materials, and 5% minerals. An intravenous nutritional regimen aims to supply all the nutrients that would be consumed or considered essential in a normal diet. Each regimen is individually tailored to meet the requirements of particular patients. It will be designed to contain the correct amounts of water, protein, carbohydrate, fat, electrolytes, trace elements and vitamins. The feeding regimen is designed to account for baseline requirements due to the disease process. Taking each of the components in turn:

Fluids

Fluid requirement must be determined based on the patient's specific clinical problems, calculated losses, and other abnormalities. Water is the principal component of the human body and accounts for more than 50% of total body weight.

The maintenance or baseline requirements for the volume of fluid required can be estimated using the formula shown below:

Ml / day = 1500 ml + 20 (body weight – 20 kg)

For example, for a 70 kg man: Fluid requirement = 1500 + 20 × (70 – 20) = 2500 ml / 24

Alternatively an estimate of requirements can be made by assuming a baseline requirement of 30 to 35 ml/kg, i.e. 70× 35 = 2450ml. It should be stressed that these are estimated requirement will be tailored to the individual during the initial course of feeding. The estimated fluid requirement is based on loss of 1500 ml in urine, 200 ml in faeces, 400 ml via sweating and 400 ml from the lungs.

The lost via sweating and from the lungs is termed insensible loss. A small volume, approximately 200 to 400 ml, is produced by catabolism or breakdown and utilization of body metabolic stores. A commonly overlooked source of fluid in normal individuals is that which comes from food intake, and is around 1000 ml/day. Most individuals drink an additional 1000 to 1500 ml/ day.

The baseline requirements for water will be affected by a number of factors

* Fever.
* Increased anabolism.
* High environmental temperature.
* Humidity.
* Abnormal losses form the gastrointestinal tract.
* Abnormal loss from the skin.
* Drug therapy.

Protein

Protein is given as mixtures of essential and non – essential synthetic L – amino acids, yield 4 kcal/ g . Of the 20 amino acids required for protein synthesis, 8 are considered to be essential.

Conditionally essential term has been used to describe amino acids which are normally synthesized by the body in adequate quantities except under conditions of stress when demand exceeds production.

Examples of these amino acids include glutamine, arginine, choline, taurine and S – adenosyl – L – methionine. Some amino acids which are not essential in adults are essential in infants or neonates such as histidine , cysteine , tyrosine and taurine . The amount of intravenously administered nitrogen necessary to establish positive nitrogen balance can be determined clinically in individual patients by using the factorial method. The estimated insensible loss of 5 mg / kg / day nitrogen is added to nitrogen losses measured in 24 – hour urine collections. An additional 12 mg/ kg/ day are added to replace nitrogen losses from the gastrointestinal tract. The daily nitrogen input is simply increased until calculations show a positive nitrogen balance.

The amount of protein required depends on the clinical situation and the degree of malnutrition. Protein requirements are usually prescribed in grams of nitrogen (1 g of nitrogen = 6.25 of protein). Most commercial solutions specify the strength in grams of nitrogen per litre. Many solutions are available and vary in their amino acid content and the other components they contain, such as electrolytes, glucose and antioxidants. The protein – sparing effects of parenteral delivered glucose and lipid is enhanced only when an adequate amount of protein is co – administered.

Protein is not improved by administering amino acids in excess of the baseline daily requirements for critically ill patients (e.g., 1.5 – 2 g / kg / day). The protein requirements can be estimated using the values given in Table 1.

Table 1 Daily nitrogen requirements in adult patients with altered metabolic states Patient's metabolic state Nitrogen requirement (g/kg/24h)

Table 1: Daily nitrogen requirements in adult patients with altered metabolic states Patient's metabolic state.

Patient's metabolic state	Nitrogen requirement (g/kg/24h
Basal	0.15
Catabolic	0.2
Hypercatabolic (burns / severe trauma)	0.3

Carbohydrate

Carbohydrate functions as a source of non – protein calories. Carbohydrate is usually provided in the form of dextrose, one of the isomers of glucose, which provides 3.4 cal / g.

table 2, shown in The calorie content and osmolality of dextrose solutions

Table 2: Show the energy and osmolality values of dextrose solutions.

Dextrose solution Concentration (W/v)	Energy Ke al / L	Energy (KJ /L)	Osmolality (mo sm / kg)
5 %	190	794	278
10 %	380	1588	555
20 %	760	3177	1110
50 %	1900	7942	2775
70 %	2660	11119	3885
Useful information : 1 g anhydrous dextrose provides 16 kj (3.8 kcal); plasma osmolality 282 – 295 mOsm / kg .			

The concentrated solutions are hypertonic and of low pH (pH 3 to 5) and are therefore irritant to vessel walls. They should be administered via central venous line directly into the fast – flowing blood in the right atrium to dilute the solution as rapidly as possible.

The maximum rate of infusion of dextrose is 4 to 5 mg / kg / min to prevent hyperglycemia , if more than 180 g is given day frequent.

In total parenteral nutrition regimens, it is necessary to provide adequate phosphate in order to allow phosphorylation of the glucose; between 20 and 30 mmol of phosphate is required daily. Fructose and sorbitol have been used to avoid hyperosmolar hyperglycaemic non – ketotic acidosis but other metabolic problems may occur, as with xylitol and ethanol which are now rarely used.

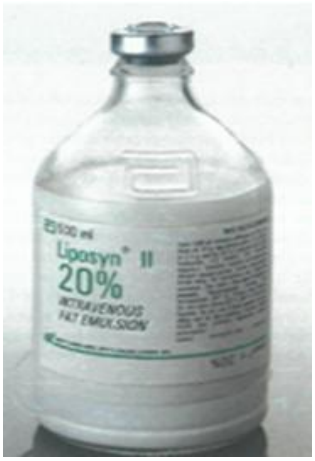
Intravenous Lipids

Lipid emulsions are required for the provision of essential fatty acids and as a vehicle for fat – soluble vitamins. In addition it is useful as a calorie source (9 kcal / g). A biochemical deficiency state may occur after 4 weeks of TPN in patients who are not given lipid. It has been suggested that 500 ml of 10% lipid emulsion infused per week is sufficient to prevent deficiency. Lipid emulsions available in UK are based on soya bean oils. They are either long – chain triglyceride (LCT) or mixed LCT and medium – chain triglyceride (MCT) emulsions. Some commercially available preparations are shown in Table 3. Lipid emulsions have the advantages of a high energy to fluid volume ratio, neutral pH and they are isotonic with plasma and can be given through peripheral vessels without causing major damage. Additives may only the mixed with lipid emulsions compatibility is known. Table 3 show Lipid emulsions used in total parenteral nutrition.

Table 3: Lipid emulsions used in total parenteral nutrition.

Solution	Kcal / L	KJ / L	Content / L
Intralipid 10 %	1100	4600	Purified soya bean oil 100 g
Glycerol 22.5 g	-	-	-
Phosphate 15 mmol	-	-	-
Intralipid 20 %	2000	8400	Purified soya bean oil 200 g
Glycerol 22.5 g	-	-	-
Phosphate 15 mmol	-	-	-
Intralipid 30 %	3000	12600	Purified soya bean
Oil 300 g	-	-	-
Glycerol 16.7 g	-	-	-

Phosphate 15 mmol	-	-	-



(fat emulsion) 20% for parenteral nutrition. *(Courtesy Abbott Laboratories, Abbott Park, Ill.)* Note that Liposyn II can be delivered by itself; it does not have to be part of TPN.

Central parenteral nutrition (CPN) permits high levels of concentration because it is infused into large veins. CPN is used for nutritional therapy needed for longer than 2 weeks. CPN maximum concentrations:

Amino acids	8.5% to 10%
Dextrose	20% to 70%
Lipids	20%

Steps in Calculation of TPN Solution

1. Energy requirement.
2. Protein requirement.
3. Amount of AA/dextrose solution.
4. Energy Provided by AA/ dextrose solution
5. Amount of energy provided by lipid.
6. Amount of lipid solution required.
7. Rate of infusion.

8. Checks for metabolic implications.
- ✓ CHO oxidation
- ✓ Lipid
- ✓ Essential Fatty Acids

9. Osmolarity *Determine route of administration
- ✓ If osmolarity is greater than 900 mOsm / L solution
- ✓ Must be administered through central vein

Injury factor
- ✓ Anabolism - 1.5
- ✓ Burn – 1.5 – 2.1
- ✓ Cancer – 1.1 – 1.45
- ✓ Closed head injury – 1.3
- ✓ Elective surgery – 1.0 – 1.1
- ✓ Fever – 1.2 per 1 degree (> 37 C)
- ✓ Major surgery – 1.6
- ✓ Mild infection – 1.2
- ✓ Moderate infection – 1.4
- ✓ Sepsis – 1.2 – 1.4 o Starvation – 0.7
- ✓ Low stress – 1.3
- ✓ Medium stress – 1.5
- ✓ High stress –

Carbohydrate

(Non – protein calories) – may be calculated using Harris – Benedict equation to estimate basal energy expenditure, then add stress and activity factors, or: Basal requirement – 25 Kcal / kg body weight

CHO intake
- Standard CHO in PN is glucose / dextrose / maltdextrose
- Range in % from 5 – 70
- Often have 50 % solution which is diluted to needs.
- Mmol/L or g/L depending on institute
- Energy content lower than expected Hydrous glucose (water associated with glucose) 16.4 kj/g or 3.48 Kcal/g usually 5.10. 15.25 % solutions
- Calculate osmolarity Percent × 50 × L 5% × 50 ×L = 250 mOsmol/L 25% × 50 × 1 = 1250 mOsmol/L 5% solution better for peripheral ¬ 5 for central catheter.

Protein – requirements usually estimated empirically
- ✓ Non – stressed 0.5 – 1g / kg body weight
- ✓ Mild stress 1.2 – 1.4g / kg body weight
- ✓ Moderate stress 1.5 – 2.0g / kg body weight
- ✓ Sever stress 2.0 – 2.5g / kg body weight Protein / amino acid solutions
- Essential and non – essential AA
- Crystalline form (pure / synthetic)

Some more soluble than others Calculating the Nutrient Content of IV solutions Example:

Patient receiving 3 liters consisting of : 1500 ml 50% dextrose (3.4 Kcal/g) 1500 ml 7% AA (4 Kcal/g) CHO : 50g/ 100 ml = x g / 1500 ml X = 750 g dextrose x 3.4 kcal/g = 2550 kcal Protein : 7g / 100 ml = x g / 1500 ml X = 150g × 4.0 kcal/g = 420 kcal Total = 2970 kcal.

Fat / lipid intake
- Good source energy, low osmolality
- Meet nutritional / energy requirements
- Emulsion used depends on assessment and plan Prevention of essential fatty acid deficiency Total nutrition support

Rate of infusion

All patients but those with fluid intolerance should initially receive two bottles of parenteral nutrition solution over the first 24 hours. This is well within the range of normal water metabolism (2000 to 2500 ml / day) and carbohydrate utilization (0.3 to 0.4 gm/ kg/ hour). After 24 hours, the volume may be increased in

increments of 1000 ml per day until the desired infusion volume is obtained (usually 2400 to 300 ml/ day). It is important that the parenteral nutrition solution be infused at a steady rate.

Large changes in the infusion rate (± 15% or more) can result in significant hypoglycemia or hyperglycemia and, if marked, in coma, convulsions , and even death . If solution administration gets ahead or behind schedule, the drip rate should not be accelerated or slowed down to meet the ordered daily volume.
Instead, the drip rate should be adjusted to the correct hourly infusion rate and continued at that rate thereafter.

Rate of flow of intravenous fluids
It should be clearly understood that the physician specifies the rate of flow of I,V, fluids in ml/ minute , drops / minute or more frequently as the approximate time of administration of the total volume of infusion . Therefore, the pharmacist may be requested to make or check the calculations involved in converting the desired total time interval into a flow of drops per minute.

STABILITY AND COMPATIBILITY IN PREPARING TPN SOLUTIONS
Preparation of TPN Solutions

Ideally, the compounding of TPN solutions would be the responsibility of a licensed pharmacist. The actual mixing can be done by a qualified technician under the supervision of a pharmacist who is familiar with aseptic manufacturing techniques. The simplest method for preparing TPN utilizes commercially available kits. The kits are designed to transfer the crystalline amino acid solution via vacuum into the partially filled 50% dextrose container.

Additives (trace elements, vitamins, electrolytes, etc.) can then be added to this base solution This system is particularly useful where there are only minimal pharmacy facilities or minimal demand for TPN. Microbial and particulate contamination is of primary concern in the preparation of any parenteral solution.

Consequently, there should be a suitable clean area designated for the manufacturing of TPN, preferably within a laminar flow hood . Through cleaning of the preparation area and regular environmental testing are essential to insure that admixtures are prepared with a minimum risk of contamination. Cleaning and testing procedures should be established for the laminar – flow hood and the surrounding buffer area.

TYPES OF INCOMPATIBILITIES
Incompatibility has been defined as phenomenon that occurs when one drug is mixed with others to produce, by physicochemical means, a product unsuitable for administration to the patient. Incompatibilities can be divided into three types: physical, chemical, and therapeutic.

Physical incompatibilities
This type of incompatibility occurs when the final solution exhibits change in appearance, such as precipitate formation, color change or gas evolution.

Chemical incompatibilities
In this type of incompatibility a formation of less active, or inactive or toxic final product occur due to component degradation in the solution.

Therapeutic incompatibilities
Therapeutic incompatibilities are more difficult to detect or study, occur when two or more drugs combine to produce an undesirable antagonistic or synergistic pharmacologic effect.

STORAGE OF MIXED TPN SOLUTION
Guidelines concerning the maximum allowable storage times and conditions for mixed – based TPN solutions (amino acids and dextrose with no other additives) are essential because it is not always practical or possible to prepare solutions immediately prior to administration. Bags which have been prepared are usually stored between 2 and 8 C until they are required.

Since TPN solutions are an excellent medium for growth of organisms and there is always a risk of introducing microorganisms into the TPN solution during mixing, there must be limitations on long – term storage.

Routine culturing of samples of solutions should be part of the microbiological control procedures of a TPN service. Ideally, TPN solutions should be administered as soon as possible after compounding, remaining refrigerated until they are administered.

Sufficient warming to room temperature will occur as the solution passes through the i.v. administration tubing to the patient.

COLOR CHANGES
Any color change or visible darkening of the base TPN solution on long – term storage makes it unacceptable for patient use even if the amino acid concentrations are within acceptable limits. The darkening, attributed to the maillard reaction, appears to be the primary route of decomposition of the carbohydrate and amino acid mixture. The color changes are progressive and range from yellow to red to dark brown. The first step in the

Maillard reaction is the formation of glycosylamines, which are generally colorless.

Therefore, color change alone is not a safe guide to the stability of the solution.

Furthermore, it should be noted that a 25% dextrose solution will normally darken itself with prolonged storage at elevated temperature, and color changes probably result from a combination of these two effects.

Electrolyte COMPATIBILITY

Precise solubility data on electrolytes in TPN solutions are difficult to determine since a vast number of electrolytes may be present in widely variable concentrations. Frequently, the pH of a TPN solution will determine whether a mixture will be compatible. Additives whose pH closely approximates that of the TPN solution are more likely to be compatible than those with different pHs.

Generally, trivalent ions from precipitates, more readily than divalent ions, which in turn from insoluble products more readily than monovalent ions, Whether or not a precipitate forms is a function of the concentration of each ion.

A precipitate may not be formed immediately, since all chemical reactions are not instantaneous.

Monovalent inorganic ions such as sodium, potassium, and chloride rarely cause solubility problems in TPN solutions. However, divalent ions such as calcium, phosphate, and carbonate can frequently cause solubility problems.

Calcium reacts with carbonates and phosphates to form relatively insoluble products. The solubility of such salts decreases with an increase in pH.

Conversely, a low pH can convert the bicarbonate ion to carbon dioxide and water. The conversion of the bicarbonate to either a precipitate or gas may be using the acetate ion as a bicarbonate precursor. Acetate salts are both soluble and stable in TPN solutions.

Calcium and Phosphorus

Calcium and phosphate will cause a solubility problem when mixed in certain ratios or when a specific mixing order is not followed. In addition, temperature, pH , amino acid concentration , amino acid products, the calcium salt, dextrose concentration, and contact with intravenous fat emulsion are factors that may affect solubility.

Usually precipitation can be avoided by adding the phosphate ion first and thoroughly mixing the solution before adding the calcium salt.

Temperature can affect the dissociation of the calcium salt. As the temperature increases, the calcium salt becomes more dissociated, providing more calcium ion to complex with phosphate. The pH of TPN is determined chiefly by the amino acid product and the dextrose concentration. If an amino acid product with the lowest possible pH is selected, more calcium and phosphorus could be administered.

The solubility of the phosphate ion itself is pH dependent. Increases in the amino concentration of TPN decrease the pH of the solution, thereby increasing the stability of calcium and phosphate. The pH of TPN decreases as the dextrose concentration increases.

This should, theoretically, increase the stability of calcium and phosphate, but this has yet to be demonstrated. It was found that higher concentrations of phosphate are attainable when calcium gluconate, instead of calcium chloride, is used as the calcium source. This is primarily because of the dissociation characteristics of the two calcium salts. Calcium chloride dissociates more readily than calcium glycinate, thereby releasing more calcium and making precipitation with phosphates more likely.

VITAMIN STABILITY

Multiple vitamin preparations are compatible at all concentrations. Vitamin A is unstable in light. If the bag is not protected with an outer wrapper or does not contain a lipid emulsion, which also provides protection against light, then estimates suggest that only 10% of the vitamin A which is added will be available at the time of infusion. Losses are reduced to about 50% if protection is employed. Artificial light has no effect, and so minimal loss occurs during the filling process.

Thiamine (vitamin B1) is the most rapidly reduced vitamin. Sodium metabisulphite and amino acids increase the degradation rate.

Ascorbic acid (vitamin C) is the most rapidly oxidized vitamin. Ascorbic acid inactivates vitamin B12 and K, and the latter two vitamins inactivate each other vitamin B12 and K should be given in separate infusions or intramuscularly.

Folic acid can precipitate in the presence of calcium salts.

Vitamins A, D, K, and riboflavin are particularly light sensitive. In order to minimize exposure during use , an overwrap may be fitted to the infusion container .

Many TPN formulations are stable for up to 90 days unless vitamins are added. Once vitamins are added, most authorities would advocate infusion within 24 hours.

INSULIN

It is well known that insulin adsorbs to the i.v. container whether it is glass or polyvinyl – chloride, to the administration se, and to the in – line filter. Nevertheless, insulin added to TPN is considered chemically stable and clinically effective in controlling TPN – induced hyperglycemia.

IRON DEXTRAN

Commercial TPN solutions already provide 0.160 to 1.36 mg of iron daily. Furthermore, iron dextran injection is not approved by the American food and drug administration (FAD) for admixture with any solution. Objection to the addition of iron include the risk of anaphylaxis and the effects of temperature, pH, light, and storage time.

HEPARIN

Heparin has been reported to be visually compatible in TPN solution in concentrations up to 2.000U/1.000 ml. However, the optimal amount, route, and method of administration to reduce the frequency and severity of thrombophlebitis and to prolong the life of the central venous line are unknown. A commonly used concentration is 1 U/ml.

ANTIBIOTICS

Because of potential protein binding, antibiotics should not be added to parenteral nutrition solutions. The penicillins are rapidly degraded by free amine. In the presence of calcium or magnesium, insoluble complexes with tetracycline may form. To insure optimal effects, all antibiotics, as well as other pharmaceuticals, should be given by separate intravenous routes.

Methods of Administration of Total Parenteral Nutrition

1. Piggy back methods

The solution with amino acids, dextrose, trace minerals, and vitamins is infused concurrently with a separate bottle of lipid emulsion through a Y site on the intravenous administration set

2. Total nutrient admixture methods

Lipids, amino acids, dextrose, electrolyte trace minerals, and vitamins are mixed in one container and administered by the central or peripheral route, depending on dextrose concentration. The method for infusion of hypertonic TPN solutions is through a subclavian vein catheter, with the tip advanced to within the superior vena cava. Other accessible veins that may be catheterized include the pectoral, cephalic, thyroid, facial, internal jugular, external jugular, and femoral veins.

Percutaneous catheterization can be performed safely in most patients by the following procedure

It is important to have expert supervision when first attempting this procedure.

1. The patient is placed supine; the head is 15 lower than the feet to promote filling and dilation of the subclavian vein by gravity.
2. A rolled sheet may be placed between the shoulders, under the thoracic vertebrae. The patient's head is turned to the contralateral side.
3. The skin of the lower neck, shoulder, and upper chest is shaved and prepared in a sterile manner.
4. The prepared area is draped using strict aseptic technique, including the use of sterile gloves and surgical instruments.
5. Local anesthetic solution is infiltrated into the skin and subcutaneous tissue at the inferior aspect of the midpoint of the clavicle.
6. A needle (5cm long, 0.5 mm in diameter) attached to a 5-ml syringe is inserted beneath the clavicle. Gentle negative pressure is applied as the syringe and needle are advanced. Venous blood in the syringe barrel indicates a punctured subclavian vein.
7. The syringe is disconnected from the needle, A flexible guide wire (J wire) is advanced through the needle into the vein while heart rate and rhythm are monitored .
8. The needle is removed. A dilator is passed over the wire, creating a suitable tract for the catheter, and then removed. A small incision may be required to facilitate initial entry of the dilator to subcutaneous tissue.
9. The TPN catheter is advanced over the wire, through the subclavian vein, and into the superior vena cava.
10. The wire is withdrawn. The catheter is left in place, with the tip resting in the middle or distal portion of the superior vena cava.
11. A syringe is attached to the catheter, and venous blood is aspirated to confirm unimpeded flow.
12. The catheter is flushed with an appropriate solution.
13. The catheter is secured firmly to the skin with a monofilament suture, and the exit site is dressed appropriately.
14. A chest X – ray must be taken to confirm correct catheter placement, before infusion of nutrient solution. After correct placement is established, infusion can begin. If the catheter is positioned incorrectly in a vein other than the superior vena cava, it should be redirected by withdrawing it 4 to 6 cm, inserting a J wire through the catheter aseptically into the superior vena cava, and advancing the catheter again over the wire. Malfunctioning central venous feeding catheters also can be replaced by inserting the J wire into the catheter, removing the defective catheter, and advancing a new catheter over the wire. Fluoroscopic guidance can be helpful in achieving and confirming optimal catheter placement, especially when placement is difficult.

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