Prevention and Management of the Complications of Total Parenteral Nutrition

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TOTAL PARENTERAL BESLENMENİN KOMPLİKASYONLARININ ÖNLEMESİ VE TEDAVİSİ

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The development of methods to provide intravenous infusion, of calories and protein has provided life saving nutritional support for critically ill patients (1), The nutritional status of such patients may have a substantial ; effect on their clinical course. The catabolic response to stress, coupled with limited intake of nutrients may cause weight loss, muscle wasting, impaired healing of soft and bony tissues, impaired immunocompetent and reduced resistance to infection (2,3,4), With the recent development of total parenteral nutrition (TPN) patients can now be adequately nourished even during severe stress.

The administration of TPN requires considerable knowledge and attention to deal il if serious complications are to be avoided (5,6). This requires a basic understanding of nutrition, biochemistry, physiology, bacteriology, pharmacology and psychology. Although TPN can be lifesaving in many situations, poor supervision may result in devastating complications, including septicaemia, metabolic derangements, biochemical imbalances and death (7,8).

To avoid or minimise complications, maximize benefits and enhance care, a TPN Consultant Service (Nutrition Team) should be designed to fit local conditions and resources. To illustrate some of the main factors, the procedures used at Addenbrooke's Hospital in Cambridge are described.

The Addenbrooke's Hospital Nutrition Team consists of a Consultant Gastroenterologist, Consultant anaesthesis , Senior Registrar in Gastroenterology, Consultant Microbiologist, Staff Pharmacist, Research Pharmacist, Nutrition Sister and Dietitian. The team deals with both enteral and parenteral feeding, including TPN solution preparation and catheter insertion. Routine aspects such as catheter care and patient monitoring are performed by the ward staff under the supervision of the Nutrition Team.

The Consultant and Senior Registrar have developed the guidelines for assessing nutritional requirements and for monitoring progress. They also supervise the team's activities.

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The Pharmacists ensure correct formulation of nutritional fluids under strictly controlled aseptic conditions and closely monitor quatily control. **In** addition they are responsible for indicating possible adverse interactions between nutrient solutions and concomitantly administered pharmaceutical preparations.

The dietitian assesses patients for enteral feeding after an initial nutritional assessment that includes evaluation of visceral and somatic proteins and **stores** of body fat. She obtains an accurate dietary **history** which is then converted to a meaningful nutrient profile. The dietitian is also responsible for weaning patients from TPN, especially when there are problems with the absorption of or tolerance to food.

The Nutrition Sister holds a central place in the team acting as a pivot for implementation of **nutri**tional support both enteral and parenteral, liaising between Nutrition Team members and ward staff, supervising the specialised nursing care of the patient and providing specialised equipment for nutritional support. She maintains permanent records, collects appropriate statistical data on septic, technicaHand metabolic complications and therapeutic results. She also participates in relevant research studies **and** undertakes nurse education for both student and qualified staff.

The team physician meets the Dietitian **and** Nutrition Sister for a daily round of all patients receiving enteral and parenteral nutritional support.

NUTRITIONAL MAINTENANCE

Administration of TPN should be considered when ever adequate nutrition cannot be maintained through the gastrointestinal tract. It should not be used if the alimentary tract is capable of absorbing adequate nutrients taken orally or infused through a nasogastric tube, expect when the patient might benefit from bowel rest (9).

Assessment of nutritional requirements of a patient, together with the planning of the daily regime and selection of appropriate nutrient solution should aim to supply :

Fluid
Energy - carbohydrate and fat
Nitrogen - amino acids
Electrolytes
Trace elements
Vitamins

An estimate of requirements of patients are determined and prescribed to Central Pharmacy. They make up appropriate solution by using Travenol ready - made standard bags to cover the whole period of 24 hours (Table 1).

Electrolytes and fluid are given according to losses or retention in the body and can be adjusted in relation to measurement of circulating electrolytes, daily full fluid intake and output. Vitamins and trace elements are given alternately to avoid possible interactions (Tables 2 and 3).

VFNOUS ACCESS (Catheter placement)

Many nutrient solutions are hypertonic and irritant to small peripheral veins. TPN should be administered through a catheter directly into a wide central vein (usually the superior vena cava or right atrium) where rapid dilution with blood reduces the damaging effect of the nutrient solution.

Table 1

Nutrients Administered in Standard TPN Regimens* (Addenbrooke's Hospital).

	Standard I	Standard II ,	Low Carbohydrate Standard I	Low Carbohydrate Standard II
Bag volume	2000 ml	2000 ml	2000 ml	2000 ml
Carbohydrate	1200 Kcals	1200 Kcals	800 Kcals	800 Kcals
Nitrogen	12.8 g	12.8 g	12.8g	12.8 g
Sodium	90 mmol	90 mmol	90mmol	90mmol
Potassium	80 mmol	80 mmol	80 mmol	80 mmol
Calcium	7.5 mmol	7.5 mmol	7.5 mmol	7.5 mmol
Magnesium	7.5 mmol	7.5 mmol	7.5 mmol	7.5 mmol
Phosphate	30 mmol	30 mmol	30 mmol	30 mmol
lipid +	10%	20%	10%	20%
Total volume	2500 ml	2500 ml	2500 ml	2500 ml
Total Energy	2110 Kcals	2460 Kcals	1610 Kcals	2060 Kcals
Trace elements ++	Standard	Standard	Standard	Standard
Vitamins 1 1 1	Standard	Standard	Standard	Standard

* The volume and the individual nutrient can be varied according to specific needs.
\+ Intralipid 10% = 550 Kcals/500 ml and 20%= 1000 Kcals/500 ml.
++ See Table 2.
+++ See Table 3.

Table 2.

Example of Trace Element Additives.

TRACE ELEMENTS	ADDENBROKE'S TRACE ELEMENTS SOLUTION/ CAMBRIDGE	ROYAL INFIRMARY TRACE ELEMENTS SOLUTION/ GLASGOW (3b).
Fe	40 umol	20 umol
Zn	100 umol	100 umol
Mn	17 umol	5 umol
Cu	32 umol	20 umol
Cr	0.4 umol	0.2 umol
Se		0.4 umol
F	120 umol	50 umol
I	2.4 umol	1 umol
Mo	_	0.2 umol

Table 3.

Examples of Vitamin Preparations for use in TPN.

		RECOMMENDED DAİLY INTAKE*
Ascorbic acid	500 mg	100 mg
Vitamin E	5 mg	10 mg
Vitamin A	10,000 iu	3,300 iu
Folic acid	0.4 mg	0.4 mg
Thiamine	40 mg	3 mg
Riboflavine	6.3 mg	3.6 mg
Pyridoxine	12.8 mg	4 mg
Niacine	100 mg	40 mg
Pantothenic acid	25 mg	15 mg
Bio tin		0.6 mg

Committe on Dietary Allowances Food and Nutrition Board (1980) (3c).

Catbeterisation, for TPN should be performed under full aseptic precautions, preferably in an operating theatre. Catheter - related complications, which remain one of the most serious problems of TPN, are reduced by using strict aseptic techniques in the insertion and subsequent management of the *line.* Passing the catheter through a subcutaneous tunnel appeals to be particularly valuable (10). Accidental or premature removal of the catheter can best be prevented by a proper suturing technique (11).

The frequency ot complications of catheter placement are inversely correlated with experience in technque, and positively correlated with emergency placement (11) Table 4). The site of the catheter Insertion should be *observed* for haemorrhage or leakage of fluid. Only saline may be infused until radiological confirmation of the catheter tip position is obtained and pneumothorax excluded by X-Ray. Pneumothorax occurs mainly after subclavian puncture. The reported frequency is in the range 0% to 9% (12). Therefore, a radiograph should he taken after insertion of the central catheter (13).

Table 4.

The More Serious Complications of Catheter Insertion,

- **Pneumothorax**
  Ilaemo thorax
- Mediastinal **haematoma**
- **Haemopericardium**
- **Hydrothorax** (intrapleural infusion)
- **Unsuccessful venipunctures**
- Arterial **punctures**
  Improperly placed catheter tips
  Air embolism
- Thoracic-duct ininiry

Infection and catheter-induced sepsis are the greatest problems in patients receiving TPN (12). There are two main sources of contamination :

a) Puncture site in the skin, where bacteria have access to the punctured vein and the circulation . In long term treatment the risk is reduced by tunneling the line to separate the puncture site in the skin from the vein.

b) The connection of the catheter to the delivery system is the other main source of contamination. Here, aspectic handing together with a change of the sterile material and restriction of the number of injections are very important.

Prevention of catheter related infections can be achieved if" the following recommendations are strictly performed i

1. The skin around the entry site should be cleaned regularly with suitable antiseptic every 24 hours using a non-touch technique.

2. The dressing used to cover the catheter insertion site should be sterile and occlusive, and should prevent movement, of the catheter in and out of the insertion site.

3. Aseptic procedures should be adopted when any part of the infusion system is handled.

4. The external line should be changed daily.

5. The catheter should be used only for TPN and not for the giving and taking of blood, administration of intravenous drugs, or measurement of central venous pressure.

6. Nothing should be added to the bag after it has been sealed by pharmacists.

Clinical signs of infection, that is, fever and chills, may be the presenting signs of a septic catheter (1,8). Sudden glucosuria and deterioration in clinical condition warrant investigation of catheter sepsis (12). If sepsis is suspected venous blood samples should be taken for culture. The patients must be carefully examined for evidence of local or systemic infection unrelated to the feeding line. If a specific cause for the pyrexia is not found, it is not unreasonable to clear the line of fibrin with urokinase followed by a short course of antibiotics (14). If signs of infection persist without obvious cause or catheter sepsis is diagnosed, the line should be removed and catheter tip and tunnel cultured. Appropriate antibiotics should be given although the infective process usually settles promptly once the line is removed. A new line can be safely established within 24 hours (14).

Several studies have addressed the problem of venous thrombosis in TPN patients. The routine addition of heparin to TPN solutions has been advocated, but *mom* recent studies have not demonstrated real advantages (16). The material of the heparinised catheters becomes stiff, increasing the risk of pressure damage to the vessel wall (17).

Silicon or polyurethane catheters with a hydromer coating rather than polyvinyl chloride or polyethylene are less likely to cause venous thrombosis (8).

Catheter occlusion occurs occasionally during TPN (12,15). It is likely if the catheter or giving set becomes kinked; if the line is left clamped for longer than necessary; when changing the giving set; or if the infusion is allowed to stop. Under these circumstances blood may clot in the catheter. If the line becomes "sticky" (i.e. shows signs of impending block) patency of catheter can be maintained by instillation of plain or heparinized saline or urokinase under the full sterile precautions. If the TPN solution is infused to quickly the line should be kept open with a slow infusion of normal saline until the next

bag is available. Ideally accurate and constant flow rates should be maintained throughout the intravenous infusion, A sudden slowing of the infusion rate may result in hypoglycemia, whereas, an increased rate of flow may cause hypeiglycaeniia or fluid overload. Irregularity of infusion can be best prevented by using a flow control device, can be best prevented by using a flow control device, such as an Imed controller, wihch monitors flow maintained by gravity, or a volumetric pump, which is independent of gravity.

Air embolism may occur as a result of the effect of negative intrathoracic pressure on the contents of a disconnected catheter. Care should be taken to ensure safe Lucr-lock connections. If the line becomes disconnected the patient should be instructed to perform the Valsalva menoevre and the foot of the bed should be elevated until the line can be clamped **(8).**

METABOLIC COMPLICATIONS

Oiniclaly important metabolic complications of TPN are related to excess or deficiency of the nutrients (18). During the early years of TPN administration, many metabolic complications were related to the inadequate monitoring of intake and imbalance of substrates, vitamins and minerals in nutrient solutions (12). During the last decade, increased knowledge of metabolism, defined requirement* for patients with various disease states, and improved patient monitoring has reduced the occurence of metabolic complications.

It is important to avoid overfeeding sick patients. Obsessional concern for maintaining or increasing body weight may lead to excess deposition of fat and a high respiratory quotient. Excess nitrogen may-exacerbate renal failure and disturb cerebration (14).

COMPLICATIONS RELATED TO CARBOHYDRATE METABOLISM

It is now generally accepted that glucose is the carbohydrate of choice for TPN. Other sugars, such as fructose and sorbitol increase the risk of lactic acidosis, cause hyperuricaemia and may be associated with a higher mortality (19). Disease states such a* diabetes meliitus, sepsis, shock or elective operations usually decrease glucose untilisation because of an increased resistance to the effect of insulin. This is in fact related to high levels of glucocorticoids and catecholamines (20). Most patients can tolerate glucose given at a rate of 0.5 g/kg body weight per hour without developing hyerglycaemia or glucosuria (18). Infusion of a larger amount of glucose may lead to hyperglycaemia, glycosuria and nonketotic coma, especially in patients with reduced glucose tolerance. It increase the production of C02 which causes a compensatory increase of minute ventilation. This in turn may aggravate a pre-existing pulmonary insffieieney or impede weaning from mechanical ventilation (18). For the average adult 400 g glucose (1600 Kcals) is the maximum permissable infusion over 24 hours. Further calorics may be given as fat (21). In patients with pulmonary deficiency and sepsis, fat emulsion is a useful source of energy (9).

In order to prevent rebound hypoglycaemia hypertonic dextrose TPN solutions should be tapered slowly before discontinuation and oral intake of food should be started 1 - 2 days before stopping TPN completely. At the beginning of TPN for hourly urine - sugar arid daily blood sugar should be carefully monitored , If hyperglycaemia becomes a problem (values persistently) more than 12-15 mm01/100 ml) the amount of glucose should be reduced and if necessary insulin administered.

COMPLICATIONS RELATED **TO** FAT METABOLISM

it is now generally acepted that intravenous fat emulsions; should be used during TPN. They not only prevent essential fatty acid (EFA) deficiency, but also provide an effective source of energy (22). Infaralipid Is the most widely used fat emulsion. It, is derived from soya bean oil and contains EPA,phosp-holipids and glycerol (21). A syndrome of EFA deficiency may develop following TPN without fat supply. Biochemical evidence of EFA deficiency has been described within 1-2 weeks following fat free TPN (23). The amount of linoleic acid required to prevent EFA deficiency in patients on TPN is not well established. One bottle of 500 ml of 10% intraiipid infused each week (corresponding to 4 gr linoleic acid per day) is sufficient to prevent EFA deficiency, a condition which may cause increased susceptibility to infection, diarrhoea and fatty infiltration of the lifer (20. Clinically significant adverse reactions include fever, headache, nausea, vomiting and muscle ache. It has been reported that fat may accumulate in the small vessels, especially in the pulmonary vasculature and that thrombocyte adhesiveness is diminished. However, none of these observations appear to have important clinical consequences (12,18).

Fat emulsions are valuable for several reasons. The low osmolarity allows safe infusion into veins; the high energy density minimises the risks of fluid overload, and the risks of EFA deficiency (9) or hyperglycaemia are eliminated or reduced. Lipid emulsions also contain vitarnen E, and may act as a vehicle for the transport of fat soluble vitamins (18). It has been shown that nitrogen losses can be minimised by the efficient use of fat as an energy substrate (25).

COMPLICATIONS **RELATED TO** AMINO ACID METABOLISM

The optimum amino acid (AA) profile for TPN is still controversial. In patients with major trauma or severe illnesses, wasting of body proteins is universal (14). Providing insufficient non-protein calories results in the infused AAs being used to meet immedi-

ate energy needs rather than for protein synthesis (20). The infusion of excess AAs increases carbamide production which in turn may cause azotaemia, and in extreme cages osmotic diuresis with dehydration. This may induce hypercalciuria with ensuing risk of negative calcium balance (18). Patients usually peresent with laboratory signs of dehydration and an elevation of blood urea nitrogen. The excretion of nitrogen in urine ig a good marker of body losses but this nitrogen represents a combination of catabolized tissue protein and deaminated dietary nitrogen (14), However, a reasonable accurate estimation of total nitrogen, loss can be obtained by measurement of the 24 hour urine urea excretion using the formula (25), Urine urea (mmol/1) x 24 hour urine volume (L) x 0.028 x 6/5 = nitrogen gr/24 hours.

Essential AAs should constitute at least 40% of the total given/and all amino acids should be in the , (L) form, since they are used much more readily than I) form AAs. The profile of non-essential AAs should be balanced, and solutions containing excessive amounts of cheap, readily available AAs (such as glycine) should be avoided. Glycine is a poor energy source and an ineffective precursor of other A A S (9).

Patients with hepatic or renal insufficiency behave quite differently from those with intact mechanisms of intermediary metabolism (14). AA solutions with modified formulae are available for patients with hepatic or renal failure (21).

COMPLICATIONS RELATED TO WATER AND MINERAL METABOLISM

During TPN, a fluid intake of 2.5 - 3.5 litres is often given, but requirements may vary. For instance, in patients with large output, intestinal fistulae or post operative drainage, several litres of fluid may be required (12). Determination of fluid can be estimated from body weight or body surface area. Unusual losses (e.g. drainage, fistulae, open wounds, burnt skin) must be replaced with appropriate electrolyte solutions. Approximate electrolyte concentrations of various body fluids are shown in Table 5, (mEq,' L>tre) (7).

Table 5.

Approximate electrolyte concentrations **of** various body fluids (rtiEq/Litre{ (7)

SOURCE	VOLUME/DAY	*m*	K	CI	HC03
Gastric	**2000** to pH<4	**60**	**10**	**90**	
	2500 **pH)** 4	**100**	10	**100**	
Pancreas	**1000**	**140**	5	75	90
Bile	1500	100	**15**	**100**	35
Small bowel	3500	**100**	15	too	25
Diarrhoea	1000 **to 4000**	**60**	**SO**	45	45
Urine	**1500**	**40**	**40**	**20**	
Sweat		**50**	**5**	**55**	

On the other hand, in patients with renal, hepatic and cardiac failure and in those with hypoalbuminaemía, fluids and electrolytes mav have to be restricted (3).

Sodium

Sodium is the main extracellular cation and is therefore important in maintaining vascular volume. It is usually not necessary to add extra sodium to the standard feeding regimen (Table 1) unless there are increased losses. By knowing the volume and type of fluid loss, the sodium requirements can be predicted (Table 5). If renal function is normal the daily excretion of sodium in urine is a useful indicator of the salt status of the body. If excess sodium is administered to a normal person it is usually excreted without difficulty. In patients with renal, hepatic and cardiac failure and in those with severe hypoalbuminaemia or recent severe injury salt excretion may be impaired.

Potassium

Most potassium is located within cells and requirements are very variable. The amount infused wiD depend on renal and gut losses as well as existing body potassium status. Potassium ion is important in glucose uptake and glycogen synthesis by cells (26), Hypokalemia can result in glycosuria in spite of adequate insulin release. To assure optimal metabolic conditions, serum potassium concentrations should be maintained in the high normal range (7). It is best guided by daily electrolyte measurements.

Calcium

Hypocalcaeniia may occur secondary to insufficient parenteral calcium supply especially in cases of concomitant vitamin D or magnesium deficiency. It recently has become apparent that metabolic bone disease occasionally results from TPN, that it resembles osteomalacia, often appears within a few months of the onset of TPN, probably appearing most- rapidly in patients whose skeletal calcium content previously had been depleted due to malabsorption (2?). Immobility increases urinary calcium losses. Whenever possible patients should be encouraged to undertake vigorous physical therapy (7).

Magnesium

Symptomatic hypomagnesaemia may develop following administration of magnesium-free or magnesium-poor TPN fluides, especially in patients with excessive gastrointestinal losses from prolonged nasogastric suction, diarrhoea! stools, entero-cutaneous fistulae, high-output enterostomies, or in patients with excessive renal losses due to a renal disorder or chronic diuretic therapy. Magnesium deficiency has a significant effect on potassium, calcium and phosphate metabolism (18). A maintenance supply of 1 0-20 rnmol per day is recommended for TPN.

Phosphate

The main cause of **hypophosphataemia** is redistribution of body phosphate. Glucose infusion results in **continuous** release of insulin stimulating **anabolism** with a rapid influx of phosphate into the muscle cells. It may uncover a depletion of phosphate in other key organs without necessarily altering total body stores. Other conditions are associated with increased renal phosphate excretion, such as alkalosis, **hypokalameia,** steroids, **hypomagnesaemia,** diuretics and diabetes **mellitus.** In most patients hypophosphataemia can be prevented **by** infusing 10-15 **mmol** phosphate per 1000 **Kcal** (28).

Zinc

During catabolism renal zinc excretion **is markedly-increased. Abnormally high zinc excretion** also occurs from the gastrointestinal system in patients with severe diarrhoea, gastric suction, fistulae and enterostomies. The symptoms of zinc deficiency may appear **within** 1-**2** months after commencement of TPN and improve dramatically upon parenteral administration of 100-300 **umol** zinc per day. Complete healing of the skin lesions is usually obtained within 10 days (18).

Very rarely, symptoms of cooper, **chromium** and **selenium** deficiency have developed in patients on prolonged TPN. In **patients with Crohn**'s disease the selenium levels fall during TPN but the significance of this finding is uncertain (29).

COMPLICATIONS RELATED TO VITAMIN METABOLISM

Vitamins are essential nutrients. There Is an increased need for water-soluble vitamins, such as thiamin **and** ascorbic acid during stress. Recently biotin deficiency has been described in a patient on long term TPN. It was associated **with loss** of hair, a rash and changes in fat distribution (18**,29),** signs which disappeared on **giving** biotin (28). For the **fat-soluble vitamins** the situation is more complex, **because** overdosage **of vitamins** A **and D may** lead **to** intoxication (18). Vitamins **A, B** complex, C, E and folic acid can **be** given, **in** TPN infusion **but B12,** d" and **K** vitamins should be given separately from TPN.

Liver Dysfunction

Minor changes in liver structure and function **are** very common during TPN. A transient rise in the level of **bilirubin,** alkaline phosphatase, **SCOT** and SGPT often occurs 1-2 weeks after starting TPN. **The** hepatic steatosis **has been ascribed to** glncoie overloading or related to EFA **deficieny.** Gallstones may also occur as a result of prolonged bowel rest, This may be **prevented** by **stimulating** gallbladder contractions using intravenous **eholecystokiriin** (80).

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