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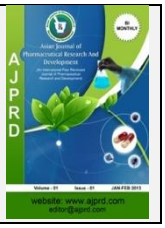

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Review Article

Metabolic Complications Associated With Total Parenteral Nutrition

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A B S T R A C T

Total parenteral nutrition (TPN) is a very important means of providing nutrients to patients who have no access to receiving nutrients by enteral route. It consists of all the essential components like lipids, protein, dextrose, electrolytes, vitamins, minerals and trace elements. The concentration of all these components can be adjusted according to the requirement of the patients. They are also available as fixed solutions. Administration of TPN requires careful monitoring as small change in concentration of nutrients in the solution may cause serious, life-threatening complications. Metabolic complications like electrolyte abnormalities, refeeding syndrome, hyperglycemia, hypertriglyceridemia and many hepatobiliary dysfunctions like steatosis, cholestasis, hepatic dysfunction and gallbladder dysfunction are all associated with the use of total parenteral nutrition.

Keywords: Total parenteral nutrition (TPN), metabolic complications, electrolyte abnormalities, refeeding syndrome (RFS), hyperglycemia, hypertriglyceridemia, hepatobiliary dysfunction.

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INTRODUCTION

TPN is defined as the intravenous (iv) administration of synthetic, balanced mixture of sterile nutrients. It is considered when all or part of the nutrients cannot be delivered by enteral means. TPN can be administered in patients with insufficient or unsafe enteral nutrition intake. Patients with non-functioning or diseased gastrointestinal tract may also depend upon this.[1] Dudrick et al, in 1967 suggested that treatment with TPN alone would be sufficientto promote normal growth and development. It was after this TPN became generally considered. By the 1970s, it was recognized as the predominant route of nutrition in patients who cannot take their daily required nutrients by the gastrointestinal route.[2]

COMPONENTS

Lipid emulsions, proteins and dextrose are the three main macronutrients present in TPN. It also contains vitamins, electrolytes, minerals and trace elements. Lipids provide about 25-30% of total calories. It also prevents the patient from fatty acid deficiency. Protein requirement for a healthy adult range from 0.8-1 g/kg/day. Patients in intensive care may need up to 1.5 g/kg/day of protein. Protein requirement varies according to the disease condition of the patient. Dextrose monohydrate serves as a source of carbohydrate.[3] Carbohydrates provide up to 60% of total calories per day. Micronutrients like vitamins and trace elements, and electrolytes such as sodium, potassium, calcium, phosphate and magnesium are given as per the requirement of the patient. While administering TPN, electrolytes should be checked routinely in order to avoid electrolyte imbalance and further problems associated with it.[4]For the administration of fluid and electrolytes, Solutions like 5% NaCl, Ringer solution, Hartmann solution, Darrow solution and 5% glucose can be used for the administration of fluid and electrolytes.[5] Patients current medical condition, comorbidities and regular medications should be assessed prior to the initiation of TPN. Before determining the nutrition composition formula, it is important to assess the patient's metabolic status and the how the disease affect metabolism.[6]

INTRAVENOUS ROUTES

TPN may either be administered via central or peripheral access, depending upon the disease condition and the treatment course.[1] Peripheral routes are preferred only for

short term therapies. Solutions with osmolarity greater than 800 mOsmol/L cannot be administered via peripheral route as it may cause thrombophlebitis or tissue necrosis. Therefore, it is important to maintain a low osmolarity of solutions (<800 mOsmol/L) when these are administered via this route.[1] Central access is preferred for both temporary or long term TPN requirement. TPN solutions with osmolarity as high as 2800 mOsmol/L can be administered via central route.[7]

ADMINISTRATION

Dietitians, doctors, nurses and pharmacists should ideally form a nutrition team in order to effectively deliver TPN. It is usually administered as a continuous infusion over 24 hours. But, once the patient regain stability, the infusion can be administered over 12-16 hours. While delivering TPN, patients' blood should be tested at intervals to monitor for electrolyte shift and hyperglycemia. Vitamins and trace elements should be monitored at the beginning of infusion.[1] However, TPN is contraindicated in patients who can receive nutrition enterally.[8]

METABOLIC COMPLICATIONS

While TPN can be a life-saving therapy for patients who cannot tolerate enteral feeding, it is associated with several metabolic complications including:

Table 1: Electrolyte Abnormalities

ELECTROLYTE	DAILY REQUIREMENT (mMol)
SODIUM	80-100
POTASSIUM	60-150
CALCIUM	2.5-5
MAGNESIUM	8-12
PHOSPHATE	15-30

TPN is associated with several electrolyte abnormalities that can have significant clinical implications.Many physiological functions, such as muscular contraction, nerve transmission, and acid-base balance depend upon electrolytes.Electrolyte abnormalities may occur when the blood levels of these minerals become too high or too low.

(A) Hypokalemia

Hypokalemia is a common electrolyte abnormality associated with total parenteral nutrition (TPN). Potassium is required for a variety of physiological activities including nerve transmission and muscular contraction. The amount of potassium in the TPN must be carefully calculated to meet the patient's individual needs, taking into account factors such as the patient's age, weight and medical condition. Another reason for hypokalemia is the quick administration of TPN. When TPN is administered too quickly, it can cause an abrupt shift of potassium from the extracellular space into the intracellular space.[9]The symptoms can vary depending upon the severity of the condition. Mild hypokalemia may not cause any symptoms, but as the potassium level in the blood continues to drop, symptoms like muscle weakness, cramping, constipation, and cardiac arrhythmias may arise. It is important to monitor the patient's serum potassium level regularly and adjust the TPN formula as needed.[10]

(B)Hypomagnesemia

Magnesium is crucial for the body's physiological functions such protein synthesis, nerve and muscle function, as well as energy metabolism. Hypomagnesemia occurs as a result of loss of magnesium through urine due to administration of TPN. This usually occurs in patients who have kidney dysfunction or who are receiving certain medications such as diuretics.[12] Symptoms of hypomagnesemia include muscle weakness, tremors, and seizures. Hypomagnesemia can also contribute to cardiac arrhythmias.[13]

(C)Hypocalcemia

TPN may cause lowering of blood calcium levelsdue to several reasons. TPN mayresult intranslocation of calcium from the extracellular fluid to cells, causing a transient drop in blood calcium levels. Some of the symptoms of hypocalcemia include cramping in the muscles, twitching, spasm, and numbness and tingling in the lips and fingers. In extreme situations, seizures and cardiac arrhythmias may also occur.[14]

(D)Hypophosphatemia

Hypophosphatemia may occur due to rapid shift of phosphate from the extracellular fluid into the cells, which can occur when patients are malnourished or have been fasting for an extended period.[15] This shift can cause a temporary decrease in blood phosphate levels. Phosphate is an essential mineral that is involved in many physiological processes in the body, including bone formation, energy metabolism, and cellular signalling. Hypophosphatemia can cause a range of symptoms including muscle weakness, bone pain, and difficulty in weaning from mechanical ventilation. In severe cases, it can lead to cardiac dysfunction and even coma.[16]

REFEEDING SYNDROME

Refeeding syndrome (RFS) is a critical condition that occurs when an individual who is malnourished begins to receive nutrition. It is a very common condition seen in patients receiving total parenteral nutrition (TPN). This syndrome can cause severe metabolic disturbances and can be fatal if left untreated. A rapid shift in the fluid and electrolyte as a result of administration of TPN is said to be the cause of this.[10] The shift is characterized by a decrease in serum electrolyte concentration, particularly phosphorus, magnesium, and potassium, as well as an increase in insulin secretion, which cause glucose uptake by cells leading to further depletion of electrolytes. Events like chronic alcoholism, severe malnutrition, prolonged fasting and metabolic stress can also cause RFS. Symptoms of RFS can be vague and nonspecific, making it difficult to diagnose.[11] Common symptoms include weakness, fatigue, confusion, dizziness, seizures, muscle cramps, and nausea. In severe cases, it can cause cardiac arrhythmias, respiratory failure, and even death. Symptoms may begin within days of starting TPN but can occur as late as several weeks. Prevention of RFS involves identifying patients who are at risk and slowly reintroducing nutrients to the body over a period of several days. Clinical manifestations of the

patients should be monitored to rule out any electrolyte disturbances. The initial dose of TPN should be low, and fluid and electrolytes should be replaced before increasing the amount of TPN administered.[15]

HYPERGLYCEMIA

Hyperglycemia is commonly seen in patients receiving TPN. It is often responsible for further complications such as dehydration, electrolyte imbalance, infections and coma in critically ill patients. TPN usually contains high levels of glucose in order to meet the energy requirements of the patients. In hospitalized patients, there are chances of hyperglycemia and fatty liver when PN solutions cross 7.2 g/kg/day. Critically ill patients, particularly those with insulin resistance or reduced glucose tolerance, may not be able to tolerate this high glucose load.[17]

HYPERTRIGLYCERIDEMIA

Hypertriglyceridemia is another complication associated with the use of total parenteral nutrition.Liver produce triglycerides in the presence of glucose and lipids. These triglycerides are released into the blood. Triglyceride levels in the blood rise due to increased synthesis of triglycerides caused by the high quantity of glucose and lipids in TPN.[18] TPN also causes hypertriglyceridemia by reducing the activity of lipoprotein lipase, which is an essential enzyme required in the breakdown of triglycerides, thereby reducing its clearance. Hypertriglyceridemia is responsible for a range of complications including pancreatitis which is a life-threatening condition, fatty liver, insulin resistance and cardiovascular disease. Monitoring triglycerides levels in patients receiving TPN is very necessary in order to adjust the composition of TPN and thereby avoid risks associated with it. This include lowering the concentration of glucose and lipids in the TPN solution.[19]

HEPATOBILIARY DYSFUNCTION

Hepatobiliary dysfunction is a potential complication associated with total parenteral nutrition (TPN). The liver and biliary system play a crucial role in processing and excreting nutrients from TPN, and any disruption in this process can result in hepatic and biliary dysfunction.[20] Some examples of hepatobiliary dysfunction associated with TPN are:

Cholestasis: Cholestasis is a condition where bile flow from the liver to the intestine is impaired, leading to the build-up of bile acids and other substances in the liver. Cholestasis can occur with TPN due to various factors such as use of high-fat solutions, lack of enteral feeding, and prolonged TPN administration. Symptoms of cholestasis include jaundice, itching, and fatigue.

Steatosis:In steatosis, extra fat builds up in the liver, causing inflammation and damage. High glucose and lipid content of TPN can also cause steatosis, which overload the liver's metabolic capacity. Symptoms of steatosis include abdominal pain, nausea, and fatigue.

Hepaticdysfunction: TPN can also cause general liver dysfunction, which can be indicated by elevated liver enzymes, abnormal bilirubin levels, and changes in liver function tests. Chronic use of TPN can cause various liver conditions like liver fibrosis, liver cirrhosis and if untreated, liver failure.

Gallbladderdysfunction: Enteral feeding is necessary in order to stimulate gallbladder stimulation and bile secretion. Patients receiving TPN lack enteral feeding, which results in gallbladder dysfunction. Gallbladder dysfunction can further cause gallstones formation and cholecystitis.

CONCLUSION

Use of total parenteral nutrition can result in various metabolic complications. Electrolyte abnormalities involving derangement of sodium, potassium, magnesium, calcium and phosphate are the most common complications. Refeeding syndrome is a critical condition caused by the fluid and electrolyte shift that may occur due to the administration of TPN. Hyperglycemia and hypertriglyceridemia are also seen in a large number of patients. TPN can also alter liver and biliary functions of the patients leading to conditions like steatosis, cholestasis, hepatic dysfunction and gallbladder dysfunction. Hence, patients receiving TPN should be carefully monitored.

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