Carbohydrates – Guidelines on Parenteral Nutrition, Chapter 5

Kohlenhydrate – Leitlinie Parenterale Ernährung, Kapitel 5

Abstract

The main role of carbohydrates in the human body is to provide energy. Carbohydrates should always be infused with PN (parenteral nutrition) in combination with amino acids and lipid emulsions to improve nitrogen balance. Glucose should be provided as a standard carbohydrate for PN, whereas the use of xylite is not generally recommended. Fructose solutions should not be used for PN. Approximately 60% of non-protein energy should be supplied as glucose with an intake of 3.0–3.5 g/kg body weight/day (2.1–2.4 mg/kg body weight/min). In patients with a high risk of hyperglycaemia (critically ill, diabetes, sepsis, or steroid therapy) an lower initial carbohydrate infusion rate of 1–2 g/kg body weight/day is recommended to achieve normoglycaemia. One should aim at reaching a blood glucose level of 80–110 mg/dL, and at least a glucose level <145 mg/dL should be achieved to reduce morbidity and mortality. Hyperglycaemia may require addition of an insulin infusion or a reduction (2.0–3.0 g/kg body weight/day) or even a temporary interruption of glucose infusion. Close monitoring of blood glucose levels is highly important.

Keywords: glucose, fructose, non-protein calories, hyperglycaemia, insulin

Zusammenfassung

Die wichtigste Rolle der Kohlenhydratzufuhr bei parenteraler Ernährung (PE) ist die Bereitstellung von Energie. Bei jeder PE sollten Kohlenhydrate infundiert werden, zur Verbesserung der Stickstoffbilanz möglichst gemeinsam mit Aminosäuren und Fettemulsionen. Während Glukose als Standardkohlenhydratlösung eingesetzt wird, kann der Zuckeraustauschstoff Xylit nicht generell empfohlen werden. Fruktoselösungen sollten keine Verwendung in der PE finden. In der Regel sollten etwa 60% der Nichteiweiß-Energie als Kohlenhydrate zugeführt werden mit einer Zufuhrrate von 3,0–3,5 g/kg KG/Tag (2,1–2,4 mg/kg KG/min). Patienten mit einem hohem Hyperglykämierisiko (kritisch Kranke, Diabetes, Sepsis, Steroidtherapie) sollten eine niedrigere initiale Kohlenhydratzufuhrrate von 1–2 g/kg KG/Tag erhalten. Die Einhaltung einer Normoglykämie ist anzustreben. Der Zielbereich für die Blutglukosespiegel ist 80–110 mg/dl, aber zumindest sollten Werte unter 145 mg/dl erreicht werden um Morbidität und Mortalität zu verminderen. Eine Hyperglykämie kann eine Insulingabe und eine Reduktion der Kohlenhydratzufuhr mit der PE auf 2–3 g/kg KG/Tag oder auch eine zeitweilige Unterbrechung der Kohlenhydratinfusion erfordern. Engmaschige Blutzuckerkontrollen sind unbedingt erforderlich.

Schlüsselwörter: Glukose, Fruktose, Nicht-Eiweiß-Kalorien, Hyperglykämie, Insulin

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Physiology

Introduction – basics

Knowledge of the biochemistry and physiology of carbohydrate metabolism is fundamental in understanding the role of carbohydrates and their critical use. The main role of carbohydrates in the human body is to provide energy. Carbohydrates also occur in the human body bound to proteins (proteoglycans), as amino sugars (glucosamine) or in a complex form as components of matrix structures. Carbohydrates are comprised of carbon (C) and water (H_2O), hence their name.
The regulation of the serum glucose level plays a central role and is influenced by various factors: *glucose intake* (enteral, parenteral); *glucose oxidation* in glycolysis or pentosephosphate cycle; *gluconeogenesis* mainly in the liver (but also occasionally in the kidneys); *glucose exchange* with glycogen stores in the liver and muscles.

Glycolysis

In aerobic conditions, glycolysis is the first step in the process of glucose oxidation. In this 2 moles of pyruvate (C3) are generated in cytosol from one mole of glucose (C6) and 2 moles of adenosine triphosphate (ATP) are released.
Under aerobic conditions, complete oxidation of the 2 moles of pyruvate through the Krebs cycle yields 30 moles of ATP. Therefore, complete oxidation of one mole of glucose to water and CO2 yields 36 moles of ATP and 2 moles of guanosine triphosphate (GTP). However, under anaerobic conditions only 2 moles of ATP are generated, and lactate is produced. Six moles of ATP are required to synthesize one mole of glucose from lactate (Cori cycle), so there is a net consumption of 4 moles of ATP. Humans with normal metabolism utilise approximately 4–5 g/kg body weight/day of glucose for glucose oxidation. Additional glucose intake results in lipogenesis, with the synthesis of triglycerides.

Gluconeogenesis and hepatic glucose production

Glucose can be synthesised in the liver or, to a lesser degree, in the kidneys. Substrates for gluconeogenesis are lactate and pyruvate, which are derived from either anaerobic glycolysis or the degradation of glucogenic amino acids (e.g. alanine, valine) from the muscles. Alanine can also be generated through the transfer of an amino group from another amino acid (especially branched-chain amino acids), to pyruvate.
The hepatic glucose production in a healthy person amounts to a maximum of 2.2 mg/kg body weight/min which is equivalent to 3.2 g of glucose/kg body weight/day. This amount equals approximately 220 g of glucose in a person weighing 70 kg. Gluconeogenesis is an energy and oxygen consuming metabolic pathway, which accounts for 50% of the hepatic oxygen utilisation. *Invivo*, gluconeogenesis and glycolysis take place simultaneously, and are arranged in a zonal fashion within the liver. The hormonal situation of the body determines which of these metabolic pathways prevail.

Hormonal regulation of carbohydrate metabolism

Under normal metabolic conditions, carbohydrate metabolism is regulated predominantly by the interaction between insulin and glucagon. Other important factors in the regulation of carbohydrate metabolism are hormones (epinephrine, cortisol) and cytokines (e.g. IL-6), particularly during post-aggression metabolism. In certain tissues, glucose uptake into the cell is insulin-independent (e.g. erythrocytes, renal medulla, bone marrow, leukocytes and brain).
Insulin lowers the intracellular concentration of glucose through genetic induction of key enzymes of glycolysis and down-regulation of key enzymes involved in gluconeogenesis. Insulin/insulin+glucose have one effect, and cAMP (acting as an intracellular agent for the glucagon) or cAMP and corticosteroids have the opposite effect in carbohydrate metabolism. Insulin also ensures that the glycogen stores in the liver and muscle cells are replenished. There is a simultaneous reduction in proteolysis in peripheral muscle cells, which provides the precursors for gluconeogenesis. Insulin, therefore, acts as an anabolic hormone.

Supply of carbohydrates

Carbohydrate application

- Carbohydrates should always be infused with PN (A).

Commentary

Carbohydrates, a key substrate in PN, can improve the nitrogen balance by exerting a protein-saving effect [1], [2], [3], [4], [5] (Ib). This can be promoted most effectively by combining the intake of amino acids with carbohydrates, or of amino acids with carbohydrates and lipid emulsions [5], [6], [7], [8], [9], [10]. Carbohydrate solutions are not only used for nutritional purposes but also for fluid replacement [11].

Types of carbohydrates to be administered

- Glucose should be infused as a standard carbohydrate solution (C).
- The use of xylite is not generally recommended due to controversial data (C).
- Fructose solutions should not be used for parenteral nutrition (A).

Commentary

The standard parenteral carbohydrate solution is glucose. Glucose is easy to measure in blood and urine for the purpose of monitoring, and prevention of overdosage.
Fructose, an important carbohydrate in a regular diet, can be partially metabolised in the body independent of insulin. In the past, fructose was often used to provide high-calorie nutrition to critically ill patients or diabetics, to prevent the complication of hyperglycaemia without insulin administration [12] (Ib). However, the use of fructose to prevent complications is now less common due to a decrease in the recommended carbohydrate or energy intake [12], [13], [14], [15] (Ib). Life threatening complications may arise in the event of a undiagnosed hereditary fructose intolerance [16].
Xylite, a sucrose substitute, can be metabolised independent of insulin in the pentosephosphate cycle. However, xylite administration results in lower concentrations of glucose and insulin even during sustained endogenous lipolysis due to its insulin-independent metabolism. The effects of xylite administration on functional proteins have been described, although not substantiated by clinical outcome parameters. Xylite, therefore, is not recommended in everyday use, due to dosage limitations and time-consuming monitoring [12], [13], [14].

Carbohydrates and blood glucose level

- As a rule approximately 60% of non-protein energy should be supplied as carbohydrates (C).
- The aim is to maintain normoglycaemia (A).
- The blood glucose level should be maintained between 80–110 mg/dL, if suitable to the overall clinical situation (A). At least a glucose level of <145 mg/dL should be achieved, because levels above 145 mg/dL have been associated with higher morbidity and mortality (A).

Commentary

Hypoglycaemia can be prevented by intake of carbohydrates in situations with reduced gluconeogenesis (e.g. restricted liver function). In order to maintain normoglycaemia, the exogenous intake should at least correspond to the rate of the normal endogenous glucose production of 2–3 g/kg body weight/day (1.4–2.1 mg/kg/min). If a higher amount of glucose is infused, the proportion of glucose utilised for oxidation decreases, whereas a higher proportion of glucose is stored as fat [6], [17] (Ib).
Approximately 60% of non-protein energy should be supplied as carbohydrates, with 4 g/kg body weight/day (2.8 mg/kg/min) being the upper limit of supply. An intake of 3.0 and 3.5 g/kg body weight/day (2.1–2.4 mg/kg body weight/min) is preferable. The endogenous glucose production in critically ill patients is not reduced by a higher infusion of exogenous carbohydrates or lipids [6], [18]. In these patients the risk of hyperglycaemia is increased. Therefore, an initial low carbohydrate infusion rate of 1–2 g/kg body weight/day should be selected for these or other patients with a high risk of hyperglycaemia (diabetes, sepsis, steroid therapy) [19]. It should also be noted that glucose tolerance decreases in older patients [20].
The rate of glucose infusion should be monitored by monitoring the blood glucose level, as procedures to measure glucose utilisation (indirect calorimetry) are not routinely used. In postoperative intensive care patients, maintenance of blood glucose levels between 80 and 110 mg/dL (6.1 mmol/L) were shown to be beneficial with regards to mortality and morbidity, compared to higher blood glucose levels [21], [22], [23]. A somewhat higher threshold was set for blood glucose level (145 mg/dL; 8.0 mmol/L) in another patient population where the outcome parameter was ICU mortality [24]. In a study of mixed surgical/medical patients, blood glucose levels kept at approximately 140 mg/dL or lower by use of insulin resulted in a significant improvement in mortality and morbidity as compared to a group where patients received insulin only after their blood glucose levels surpassed 200 mg/dL. A retrospective analysis of a subgroup of this population showed that the lowest mortality occurred when the blood glucose levels were kept between 80 and 99 mg/dL (4.4–5.5 mmol/L) [25]. A decrease in mortality with strict maintenance of normoglycaemia in critically ill patients only occurred when the intensive care treatment period exceeded 3 days [26]. Lowering of blood glucose levels to between 80 and 110 mg/dL was also associated with lower morbidity in critically ill patients [26]. In an analysis of surgical patients, a blood glucose level of over 110 mg/dL was associated with increased mortality and morbidity, although this effect seemed to be less marked in medical patients [22]. The positive effect on mortality and morbidity by maintenance of blood glucose levels below 145 mg/dL is undisputed in all patients subjected to prospective randomised studies. Hypoglycaemia, which occurs more often with the use of intensive insulin therapy, requires frequent checks to determine the correct insulin dose, which should be implemented with the use of an established algorithm.
Moreover, hyperglycaemia was also associated with deterioration in various acute disorders such as cerebral ischemia [27], [28], [29] or myocardial infarction [30], [31], [32], irrespective of the presence of previously diagnosed diabetes. It is likely that strict control of hyperglycaemia with insulin therapy will improve the outcome and short-term morbidity in patients with such diseases. However, there are no prospective studies addressing this issue in these patient groups.

Contraindication – hyperglycaemia

- Hyperglycaemia *may* in addition to insulin infusion require a reduction, or even a temporary interruption, of carbohydrate infusion (C).

- In order to avoid hyperglycaemia insulin administration may be necessary. This demands strict monitoring of blood glucose levels (B).

Commentary

The only contraindication for carbohydrate intake is lasting hyperglycaemia with an insulin requirement of more than 6 I.U./h. Patients with pre-existing diabetes also require carbohydrates with simultaneous insulin infusion in their PN. Insulin reduces blood glucose levels through increased cellular glucose intake and glucose turn-over. The effects of insulin may be greatly reduced in certain disorders, such as diabetes mellitus, post-operative insulin resistance, or sepsis. In hyperglycaemia, the amount of calories and carbohydrates should be restricted (reduced to 2–3 g/kg body weight/day) and insulin should be administered. Continuous intravenous insulin infusion is now preferred in intensive care patients. An intake of approximately 2–4 I.U./h is necessary as part of PN after an initial bolus has been given. The higher the insulin intake and lower the hyperglycaemia, the more frequently the blood glucose levels should be monitored. Initially, hourly to three-hourly checks are necessary (cf. chapter "Complications and monitoring" http://www.egms.de/en/gms/2009-7/000076.shtml).

Notes

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