
Review Article

Impact of neurointensive treatment on metabolism and nutrition

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ABSTRACT: Objective. To investigate the effects of neurointensive treatment on metabolism and nutrition of patients with brain injury.

Design. A systematic review of the literature.

Materials and methods. RCT, reviews, guidelines were considered and analyzed.

Results. The gastrointestinal tract dysfunctions are common and frequent findings in patients with neurological lesions. There is a significant correlation between severity of neurological damage and gastrointestinal alterations. Neurointensive drug treatments may cause metabolic and nutritional alterations too: in primis hypertriglyceridemia, hyperglycemia, electrolyte disorders. Catecholamines have marked metabolic effects, particularly on glucose metabolism with enhanced rates of aerobic glycolysis, glucose release, and inhibition of insulin-mediated glycogenesis. Insulin seems to play a role in reducing intracranial pressure. Sedation, opioids and muscle relaxants seems to have only minor effects on gastrointestinal function. Hypocapnia and calcium channel blockers seem to have only minor effects on metabolism and gastrointestinal function in patients with neurological lesions.

Conclusion. The impact of neurointensive treatment on metabolism and nutrition in patients with brain injury is demonstrated and it seems useful for prevention of secondary injury. (Nutritional Therapy & Metabolism 2008; 26: 23-31)

KEY WORDS: Metabolism, Nutrition, Neurointensive care, Neurolesion, Sedation, Opioid

INTRODUCTION

Gastrointestinal tract dysfunctions are common and frequent findings in patients with neurologic lesions. These patients do not tolerate enteral nutrition, and start presenting important metabolic and nutritional alterations. The risk of gastric content inhalation is increased, and absorption of drugs administered orally or via nasogastric tube, as well as timing and quantity of enteral nutrition, may be influenced. These dysfunctions are the result of an alteration of the brain-gut axis and gastrointestinal peptides secreted by hypothalamic-pituitary-adrenal axis. They begin immediately after injury, with incidence rate ranging from 44% to 100%.

Four aspects characterize the possible gastrointestinal changes after neurologic lesion: (a) ischemia of the gastrointestinal mucosa, with stress ulcer and gastrointestinal bleeding; (b) impaired motility with abdominal distention, diarrhea, gastric retention, and sometimes toxic intestinal paralysis; (c) destruction of the intestinal barrier with toxic and bacterial translocation, possibly

leading to systemic inflammatory response syndrome and sepsis; and (d) altered absorption of nutrients by the intestinal mucosa, possibly leading to malnutrition. However, a standardized method for measuring these dysfunctions has not yet been formulated (1-3).

These alterations and lesions develop rapidly after injury, within the first week at the latest (4). The phenomenon of delayed gastric emptying (-50% compared with physiologic levels) is more evident within the first 72 hours, and tends to decrease with time.

Several factors, such as a condition of ischemia-reperfusion, intramucosal acidosis, and incretion of cytokines and inflammatory mediators, may contribute to the development of the above conditions. There is a significant correlation between severity of neurologic damage as represented by the Glasgow Coma Score score and gastrointestinal alterations (5).

An intracranial pressure > 15 mm Hg produces an autonomic dysfunction with alteration of the biphasic gastric emptying: more rapid than the physiologic rhythm during the early phases, and more prolonged

in the late phase (6).

Neurointensive drug treatments may cause metabolic and nutritional alterations too: *in primis* hypertriglyceridemia, hyperglycemia, and electrolyte disorders. Catecholamines have marked metabolic effects, particularly on glucose metabolism with enhanced rates of aerobic glycolysis, glucose release, and inhibition of insulin-mediated glycogenesis. Insulin seems to play a role in reducing intracranial pressure. Sedation, opioids, and muscle relaxants seem to have only minor effects on gastrointestinal function. Hypocapnia and calcium channel blockers seem to have only minor effects on metabolism and gastrointestinal function in patients with neurologic lesions.

In this work we review the pharmacologic and clinical approaches to brain-injured patients, focusing attention on their effects on enteric and metabolic systems. And, we analyze why feeding these patients could be a time-consuming problem, and which kind of metabolic alterations are specifically related to the neurointensive treatment.

TREATMENTS

Neurointensive treatment

The aim of medical treatment in cases of neurologic lesions is to avoid or reduce secondary cerebral injuries. The neurologic damage is not limited to the moment of the initial injury (primary damage), but evolves during the following hours and days (secondary damage). Inotropes and vasoconstrictors are routinely used to increase inadequate Mean Arterial Pressure (PAM) levels after volemic reintegration (< 90 mm Hg), in order to improve cerebral perfusion pressure (CPP), with the aim of obtaining a CPP > 70 mm Hg.

The airway lumen must be kept free with tracheal intubation in patients in a state of coma. Adequate sedation and analgesia must be ensured during assisted ventilation. The main objectives are to control the stress response and algogenic stimulation, to guarantee endotracheal tube tolerance, to adapt to the ventilator, and to reduce nursing-induced intracranial alterations.

Patient care must include a systemic intensive gastro-protective treatment, an accurate management of the respiratory tract, maintenance of an adequate hydroelectrolytic balance, control of infections, nutritional therapy, and physiotherapy (7, 8).

Hyperventilation

Hyperventilation is often used to control intracranial pressure increases. Hypocapnia limits brain edema by re-

ducing cerebral blood flow, decreasing the total volume of the cerebral content, and, possibly, increasing cerebral oxygenation. No convincing evidence has ever been reported on prolonged hyperventilation and on hyperventilation in the absence of elevated intracranial pressure (9).

In healthy volunteers subjected to hyperventilation-induced hypocapnia, the colon tone and serum noradrenaline levels increase markedly ($p = 0.017$); conversely, splanchnic blood volume decreases significantly, by approximately 10%. These effects are not linked to incretion, rather they are the result of direct effects of hypocapnia on metabolism or of alterations in the central autonomic control on smooth muscle cells in the colon (10).

It has been demonstrated experimentally that spontaneous breathing maintained with a ventilatory support improves systemic and intestinal blood flow (11).

Hyperventilation and consequent hypocapnia may be used to maintain acceptable intracranial pressure values during neuroanesthesia and neuroresuscitation without evident effects both on systemic and on splanchnic oxygenation. Hepatic flow parameters are not significantly altered either after acute or during prolonged hypocapnia. Hypocapnia does not modify liver and splanchnic DO_2 and VO_2 levels (12).

The effect of positive end-expiratory pressure (PEEP) on splanchnic flow has been demonstrated experimentally to be dose-dependent. Levels of PEEP up to 15-20 cm H_2O determine significant decreases in splanchnic blood flow and may be compensated for by an increase in cardiac output both through volemic expansion and after inotrope administration. Splanchnic VO_2 levels are normally maintained through a corresponding, compensatory increase in O_2 extraction (13-19).

Sedatives and opioids

Sedation and analgesia are used both to control the neuroendocrine stress linked to trauma and intensive care, and to control intracranial hypertension. The most widely used sedatives are benzodiazepines, barbiturates, and propofol, while analgesia is achieved through opioids: fentanyl citrate, morphine, and remifentanyl. Analgesia and sedation involve alterations of the metabolism and of the intestinal tract, which contribute to worsening gastrointestinal functioning, already impaired by the neuroendocrine mediators triggered by the central nervous lesion.

Due to its pharmacokinetic properties, propofol (2,6-diisopropylphenol in soybean oil, glycerol, and lecithin emulsion—intralipid 10%) allows for easy management of the level of sedation and a rapid regaining of consciousness at the end of infusion. Because of its soybean oil component, in cases of continuous infusion for over

72 hours, propofol is associated with a progressive increase in triglyceride concentration. In cases of a contemporary total parental nutrition with lipid contents, the overall lipid concentration could lead to a deposit of triglycerides and of very-low-density lipoproteins VLDLs. In critically ill patients, there is a reduced capacity for lipid utilization, both as regards endogenous lipids produced by a response to the acute phase and exogenous lipids produced by hepatic alterations. Furthermore, 2,6-diisopropylphenol could play a role in this scenario, inducing an altered beta-oxidation of free fatty acids. At the end of infusion, triglyceride concentration generally reaches normal values in a few days. Hypertriglyceridemia, which may result from either 2% or 1% propofol concentrations, is an important cause of treatment failure, and indicates the need to proceed to other sedatives. Triglyceride concentration levels > 20 mmol/L may be associated with pancreatitis, central nervous system lesions, or prothrombotic effects due to an increase in factor VII and in the plasminogen activator inhibitor (20, 21).

Propofol has important antioxidant properties (its chemical structure is similar to that of some natural antioxidants, such as vitamin E): it acts as a scavenger of oxygen free radicals, reduces lipid peroxidation, decreases the activity of the glutathione peroxidase enzyme, while increasing the activity of glutathione reductase and transferase, and reduces the activity of inducible nitric oxide synthase. This occurs mostly in cases of local and systemic inflammatory response linked to ischemia-reperfusion processes. The antiinflammatory activity of propofol could also be linked to a decrease in neutrophil activity, leading to a reduced release of proinflammatory cytokines (22, 23).

Propofol infusion syndrome (PRIS), often fatal, is usually linked to prolonged high-dose infusion, mostly when associated with catecholamines in continuous and prolonged infusion as vasoconstrictor agents. Some authors report cases of early onset after only a few hours of infusion (24). The syndrome, initially described during infusion in pediatric patients, manifests itself as significant metabolic acidosis and lactic acidosis, rhabdomyolysis, hyperpotassemia, arrhythmias, and renal and cardiocirculatory failure. Most cases in adult patients described in the literature involve neurologically impaired patients, in which propofol is used at high doses to control intracranial hypertension. A possible safety margin could be identified in infusions < 5 mg/kg per hour (25, 26).

The pathogenesis of PRIS seems to be linked to a mitochondrial oxygen failure due to the quantity of lipids administered, although a recent experimental animal study demonstrates that intralipid is only minimally responsible for PRIS, while it emphasizes the key role of

propofol itself. Alterations in the oxidation of free fatty acids and the relative imbalance between energetic demand and supply lead to peripheral and cardiac muscle necrosis, with myocytolysis and rhabdomyolysis for cytopathic hypoxia (27). The disturbed transport mechanism of mitochondrial acylcarnitine caused by inhibition of its transport protein (produced, in turn, by an increase in malonyl carnitine induced by propofol) and an interruption of the respiratory chain complex 11 lead to altered fatty acid oxidation. This may lead in turn to an important energetic deficiency in cases of limited glycidic reserve (28).

Midazolam

Midazolam is one of the most widely used benzodiazepines for sedation in critically ill patients, but its use has been limited in brain trauma patients because of the wide variability in consciousness recovery times after stopping the drug infusion.

Benzodiazepines have only minor effects on gastroduodenal motility and do not influence gastric emptying in volunteers, while a recent study in mice showed inhibited gastric emptying and delayed gastrointestinal transit, by propofol and midazolam at sedative doses.

In the intensive care population, sedation (sedative agents and opioids) seems to be a risk factor for vomiting and upper digestive intolerance (29, 30). Head-injury patients are usually considered hypermetabolic. Therapeutic sedation has a major effect on the level of energy expenditure (EE), as demonstrated in several studies. For example, Bruder et al studied 8 patients in the early (first week) and late (second-fourth week) stages after their brain trauma: they found that EE was significantly lower in the first measurements, when all patients were sedated with fentanyl + flunitrazepam and mechanically ventilated, than in the second period, when no patients received any sedative and all were spontaneously breathing ($EE = 1,737 \pm 71$ vs. $2,121 \pm 194$ Kcal/day) (31). Similar results were found by Bardutzky et al in 34 patients with acute stroke, who were sedated (fentanyl + midazolam), mechanically ventilated, and monitored continuously from day 1 through day 5 after intensive care unit admission: EE varied from $1,560 \pm 240$ to $1,623 \pm 251$ Kcal/day (32).

Thiopental

Brain-injured patients are susceptible to secondary brain damage related to decreased CPP associated with edema and increased intracranial pressure. Whenever conventional therapy fails to reduced elevated intracranial pressure, barbiturate coma represents an additional intervention for refractory intracranial hypertension. In a

recent study, patients with pentobarbital-induced coma developed a significant ileus and consequently did not tolerate enteral nutrition. Improvement in feeding tolerance is seen when the postpyloric route is used. But whether feeding intolerance is mainly due to barbiturates or related to traumatic brain injury is not always clear (33).

Patients treated with barbiturate coma seem to present a higher incidence of adrenal insufficiency compared with controls (53% vs. 22%, $p = 0.03$), which is associated with a need for higher doses of norepinephrine to maintain CPP than is the case in patients treated with barbiturates without adrenal impairment (1.07 ± 1.04 vs. 0.31 ± 0.32 $\mu\text{g}/\text{kg}$ per minute, $p = 0.03$) (34).

Opioids

It is well known that opioids suppress bowel function, even during short-term therapy. Opioid bowel dysfunction (OBD) is a common adverse effect associated with opioid use, characterized by constipation, abdominal distension, increased gastric reflux, nausea, and vomiting. The mechanisms for OBD have been linked to delays in gastric motility and emptying, inhibition of small and large intestinal propulsion, and diminished enteric secretions. These effects are predominately mediated through peripheral (gastrointestinal) μ -receptors, with only minor central nervous system-mediated effects (35, 36).

In mechanically ventilated critically ill patients, surgical patients, and healthy volunteers, continuous infusion of opioids leads to alterations in gastroduodenal motility that prevent easy enteral nutrition, because of gastric retention, vomiting, abdominal distention, and delayed peristalsis (37, 38).

Heyland et al, in their prospective study of 72 mechanically ventilated critically ill patients, found better gastric emptying in patients who were not treated with opioids, and, moreover, higher doses of opioids were associated with a greater impairment of gastric emptying. As a consequence, strategies to minimize the use of narcotics may improve gastric motility (39).

In patients with head injuries, the situation seems to be different: avoiding the use of morphine does not lead to any improvement in gastric emptying, measured both with a paracetamol test and through residual volume after a test bolus in enteral nutrition.

McArthur et al compared gastric emptying in ventilated, brain-injured patients sedated with either an opioid-based regimen (morphine plus midazolam) or propofol. They failed to demonstrate any improvement in gastric motility in the propofol group, as assessed by paracetamol absorption and by residual volumes following a test feed. This study found an association between intracranial hypertension and reduced gastric emptying, in-

dicating that brain injury may directly affect tolerance to enteral feeding (40). One of the possible explanations for this lies in the kind of alterations of gastrointestinal function typical of neurologically impaired patients: neurologically induced alterations are likely to have earlier onset and greater intensity as compared with those induced by opioids: so opioid's avoidance is completely useless for restoring intestinal functions.

Neuromuscular blocking agents

Muscle relaxants are used in intensive care in brain-injured patients to facilitate ventilation and to control intracranial pressure. The administration of neuromuscular blocking agents causes a significant decrease in the energy expenditure of severely head-injured adults, as demonstrated by McCall et al. In their study, neuromuscular blockade given with morphine eliminated the hypermetabolism associated with head injury, as measured energy expenditure was only 95% of the predicted (41).

Muscle relaxants do not affect gastric emptying and enteral absorption, and effective enteral nutrition support has been provided safely to patients under sedation and neuromuscular blockade, as shown by Tamion et al in a critically ill population (42).

Antiedema therapy

In clinical practice, mannitol has replaced other osmotic diuretics administered to reduce increased intracranial pressure (43). The mechanisms involved are systemic hemodynamic (volemic expansion, lowered hematocrit and blood viscosity levels, and increased cardiac output and arterial pressure), cerebral (increased cerebral blood flow, in particular within the microcirculation; and decreased intracranial pressure), and an osmotic diuretic effect (effects on proximal tubular cells, where osmotic pressure is exerted which is vigorous enough to prevent the reabsorption of solutes and water) (44, 45). The effects on cerebral blood flow seem to be more striking in patients with CPP < 70 mm Hg.

Mannitol leads to a decrease in intracranial volume, both by attracting water back to the vessels through the gradient of osmotic pressure in regions with an intact blood-brain barrier, through arterial vasoconstriction, and through a decreased production of cerebrospinal fluid. It may penetrate a damaged blood-brain barrier, and repeated administration in the presence of accumulations may worsen intracranial pressure due to an inversion of the osmotic gradient. The antiedemigenous effect is evident 15-30 minutes after infusion, and lasts 90 minutes to 6 hours. The osmotic shift through which mannitol decreases extracellular and maybe also intracellular volume

could be responsible for the reduced extracellular space. This could lead to an increase in the concentration of glucose, lactate, pyruvate, and glutamate molecules, which are not eliminated from the affected areas, thus starting a nonspecific dehydration (46).

Mannitol is a metabolically inert alcohol; however, it may produce hyponatremia, hypobicarbonatemia, hypocalcemia, hypophosphatemia, metabolic acidosis, and/or dehydration. These phenomena are more frequent and plausible in cases of increased blood pool concentration. Variations in the glomerular renal flow may account for an increase in $t_{1/2}$ from 39 to 103 minutes with a 0.5-0.7 g/kg dose. (44)

Mannitol should not be administered when osmolality is > 320 mOsm (47). It has potential nephrotoxic effects: the incidence of acute renal failure ranges from 11.6% to 76%, according to the clinical setting, and the definitions and methods followed (48, 49). This risk is increased further if nephrotoxic drugs (e.g., antibiotics or vasoconstrictors) are administered at the same time, as well as in cases of sepsis or in the presence of concurrent diseases linked to hypertension, heart failure, diabetes, or high APACHE 2 scores. These mechanisms are probably linked to arterial vasoconstriction, tubular vacuolation, tubular cell swelling, increased intraluminal sodium concentration at the level of the macula densa, and increased oncotic pressure. However, the 320 mOsm threshold used in clinical practice does not seem to be correlated to mannitol-induced renal failure (48); in 30%-40% of measurements exceeding this threshold value, renal dysfunction was not observed (50).

Vasopressor therapy and Triple H

The use of vasopressors as a component of the so-called Triple H therapy (hypertension, hypervolemia, and hemodilution) is widespread in clinical practice, although no significant evidence has been reported for benefits in terms of reduced ischemia or mortality (51, 52).

The endocrine reaction to a stressful challenge consists in the activation of the sympathoadrenal and the hypothalamic-pituitary-adrenal axis, leading to increased plasma levels of catecholamines and glucocorticoids, both of which help induce hyperglycemia. The counter-regulatory hormones (norepinephrine, growth hormone, and glucagons) inhibit hepatic glycogenesis and peripheral glycolysis while promoting gluconeogenesis, hepatic and muscle glycogenolysis, and peripheral lipolysis. Peripheral glycolysis and the breakdown of glycogen, lipids, and, later, muscle protein provide the substrates for hepatic gluconeogenesis in the form of pyruvate, glycerol, and alanine. Proinflammatory cytokines such as TNF- α and IL-6 were both shown to have the potential

to induce a state of peripheral and hepatic insulin resistance. Increased gluconeogenesis fueled by proteolytic, lipolytic, and glucolytic metabolites combined with hepatic insulin resistance are considered the main causes of stress-induced hyperglycemia, but more factors such as exogenous dextrose, enteral or total parenteral nutrition, age, diabetes, and bed rest can further aggravate this picture (53).

Catecholamines are once the drugs of choice to treat hypotension during shock states; however, they also have marked metabolic effects, particularly on glucose metabolism. The degree of this metabolic response is directly related to the β 2-adrenoreceptor activity of the individual compound used. Under physiologic conditions, infusing catecholamine is associated with enhanced rates of aerobic glycolysis (resulting in adenosine triphosphate production), glucose release (both from glycogenolysis and gluconeogenesis), and inhibition of insulin-mediated glycogenesis. Hyperglycemia and hyperlactatemia are the hallmarks of this metabolic response. Under pathophysiologic conditions, the metabolic effects of catecholamines are less predictable because of changes in receptor affinity and density and in drug kinetics and the metabolic capacity of the major gluconeogenic organs, both resulting from the disease per se and the ongoing treatment. It is well-established that shock states are characterized by a hypermetabolic condition with insulin resistance and increased oxygen demands, which coincide with both compromised tissue microcirculatory perfusion and mitochondrial dysfunction. This causes impaired glucose utilization and may lead to inadequate glucose supply and, ultimately, metabolic failure (54).

Respiratory chain activity is responsible for the generation of a transmembrane potential across the inner membrane (Δp) that is involved in calcium homeostasis and reactive oxygen species production, in addition to adenosine diphosphate phosphorylation. Mitochondria play a major role in cell signaling pathways in relation to several cellular key functions, including transcriptional responses and cell death commitment. In the substrate metabolism for energy production, glucose oxidation has a more efficient oxidative metabolism as compared with fatty acids. Hence, although palmitate does contain more energy per gram of substrate (9.69 Kcal/g) as compared with glucose (4.81 Kcal/g), it consumes more oxygen to produce 1 adenosine triphosphate molecule. This indicates that when oxygen is not limited, lipids are the most appropriate substrate for high and sustained adenosine triphosphate supply. Conversely, if oxygen is a limiting factor, as it is in several diseases with low oxygen delivery/consumption, glucose oxidation seems to be the best choice because of higher efficiency of adenosine triphosphate synthesis (55).

Studies on animal models of hypoxia-ischemia and traumatic brain injury have revealed significant reductions in mitochondrial oxygen consumption, enzymatic activity (cytochrome oxidase and succinate dehydrogenase), and membrane potential. Additionally, clinical investigations in severely head-injured patients have shown increases in brain extracellular lactate levels despite well-preserved regional blood flow and brain tissue oxygen tension, thus indicating a stimulation of anaerobic glycolysis due to inefficiency of the mitochondrial oxidative metabolism (56).

Based on the landmark studies on intensive insulin use, a crucial role is currently attributed to glucose homeostasis. In 63 isolated brain-injury patients, intensive insulin therapy reduced mean ($p = 0.003$) and maximal ($p < 0.0001$) intracranial pressure while identical CPPs were obtained with 8-fold less vasopressors ($p = 0.01$). Seizures ($p < 0.0001$) and diabetes insipidus ($p = 0.06$) occurred less frequently. At 12-month follow-up, more brain-injured survivors in the intensive insulin group were able to care for most of their own needs ($p = 0.05$) (57).

Vespa et al demonstrated that intensive insulin therapy was associated with an increased incidence of microdialysis markers of cellular distress, namely elevated glutamate ($38\% \pm 37\%$ vs. $10\% \pm 17\%$, $p < 0.01$), elevated lactate/pyruvate ratio ($38\% \pm 37\%$ vs. $19\% \pm 26\%$, $p < 0.03$), and low glucose ($26\% \pm 17\%$ vs. $11\% \pm 15\%$, $p < 0.05$), and increased global oxygen extraction fraction. Mortality was similar in the intensive and loose insulin treatment groups (14% vs. 15% , $p = 0.9$), as was 6-month clinical outcome ($p = 0.3$) (58).

Systemic changes in blood pressure and cardiac output induced by pressors and inotropes do not always correlate with improvements in regional perfusion. Norepinephrine has a minimal impact on mesenteric blood flow, although the combination of norepinephrine and dobutamine increases splanchnic blood flow in sepsis. Dopamine also increases mesenteric blood flow although this may be associated with negative hepatic energy balance at high doses (59).

Elevated plasma noradrenaline concentrations alter gastric secretion, but it is probable that they interfere with other variables such as blood flow, bicarbonate secretion, or prostaglandin synthesis (60).

Catecholamines stimulate the growth of various gram-positive and gram-negative bacteria, including *Pseudomonas aeruginosa*, *Yersinia enterocolitica*, *Salmonella enterica*, *Listeria* spp., *Bordetella* spp., and *Staphylococcus* spp. Noradrenaline stimulates the production of *Escherichia coli* O157 virulence factors in vitro. It also increases the adherence of this bacterium to tissue in vivo and stimulates enteritis in a bovine intestinal loop model (61).

Calcium channel blocker therapy

Calcium channel blockers (also known as calcium antagonists) reduce the influx of calcium into the cell by blocking the calcium channels. Their use has been suggested for prevention or treatment of cerebral vasospasm after brain injury, based on the hypothesis that these drugs can counteract the influx of extracellular calcium in the vascular smooth muscle cells and prevent the blood vessels constricting. Nimodipine binds specifically to L-type voltage-gated calcium channels. There are numerous theories about its mechanism in preventing vasospasm, but none have been demonstrated conclusively (62).

Nimodipine influences the levels of circulating corticosterone under most conditions except those of extreme stress. It alters the balance between mineralocorticoid and glucocorticoid receptor occupancy that would occur in the absence of the drug, and it alters the genomic post-translational and membrane actions of the adrenal hormones (63).

CONCLUSIONS

Brain injury directly affects the enteric system, and neurointensive treatment leads to metabolic alterations that can deteriorate already impaired gastrointestinal functions. Brain-injured patients are at high risk of developing gastrointestinal tract dysfunction, intolerance to enteral nutrition, and malnutrition.

In light of these facts, the approach to artificial nutrition in patients with central nervous lesions should be managed with great attention, including early enteral nutrition if possible, careful monitoring of feeding tolerance, and consideration given to implementing caloric and proteinic intake with parenteral nutrition if needed.

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