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ABSTRACT

Patients with acute neurological diseases (traumatic brain injury, hemorrhagic or ischemic stroke, spinal cord injury or tumour) may present with various systemic alterations such as changes in cardiovascular and respiratory response, gastrointestinal function disorders, metabolic and endocrinological abnormalities, coagulopathies, among others. Head injury increases the risk of malnutrition due to multiple factors related to nutrient intake, abnormalities in energy expenditure, eating behaviour disorders, gastrointestinal changes, and medication side effects.

Keywords

traumatic brain injury,
gastrointestinal tract,
gastroparesis,
delayed gastric emptying



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Gastrointestinal conditions include gastroparesis, which is defined as a delay in gastric emptying in the absence of mechanical obstruction. These patients often report nausea, vomiting, pain, postprandial fullness and abdominal swelling. Although the exact mechanism by which it occurs in traumatic brain injury is not known, it is related to complications such as intracranial hypertension, so it is most often seen in cases of severe trauma. Therefore, the objective of this review is to expose basic and practical concepts about gastroparesis and its approach.

INTRODUCTION

Traumatic brain injury (TBI) is one of the most frequent acute brain pathologies that constitute a serious public health problem worldwide due to its high mortality and number of cases of permanent disability after its occurrence [1]. The most recent data provided by the Centers for Disease Control and Prevention (CDC) estimates that for the year 2019 there were about 61,000 TBI-related deaths in the United States, which is approximately 166 deaths every day [2]. This condition can be caused by a blow, jolt or penetrating head injury that disrupts the normal functioning of the brain [2]. TBI, especially severe TBI (Glasgow Coma Scale < or equal to 8), is associated with many consequences, the most common being altered consciousness, coma, movement and gait disorders, memory impairment - learning, among others; however, the occurrence of gastrointestinal dysfunction in patients, such as gastroparesis, has been reported days after traumatic brain injury [3].

The incidence of gastroparesis (GP) in TBI ranges around 45-50%, and is closely related to the severity of trauma and intracranial hypertension [4]. GP is a well-documented finding among patients with severe TBI [5]. GP is defined as delayed gastric emptying in the absence of mechanical obstruction [6-8]. In these patients, a temporal profile of delayed emptying has been described during the first 2 weeks post-trauma with subsequent improvement [4]. Although the exact cause of GP in TBI is unknown, altered nerve signaling to the stomach appears to be a factor [9]. Other factors that promote its onset are inflammation, sepsis, hydroelectrolytic alterations (hypokalemia, hypomagnesemia), hyperglycemia, frequently used drugs (opioids, furosemide, hydantoin, antacids, corticosteroids, among others), renal and hepatic dysfunction, and liver dysfunction [4,6].

Considering the relevance of this topic in the care of the neurocritical patient and the lack of current evidence to know the impact of this condition, the objective of this review is to present basic concepts related to the pathophysiological process, general approach and future perspectives of gastroparesis in patients with traumatic brain injury.

GENERAL INFORMATION ON GASTROPARESIS IN PATIENTS WITH TBI

It has been shown that more than 50% of patients with severe traumatic brain injury do not tolerate enteral feeding, which presents itself in the form of vomiting, abdominal distension, delayed gastric emptying, esophageal reflux and decreased intestinal peristalsis [10]. The above suggests that gastrointestinal dysfunction is a frequent entity following TBI and that the association between the severity of brain injury and enteral feeding intolerance appears to be related to the existence of a link between the central nervous system and the non-functioning gut [10].

As mentioned above, one of the factors involved in such intolerance consists of delayed gastric emptying or gastroparesis [11]. Gastroparesis and altered gastric accommodation are the result of a neuromuscular dysfunction of the stomach. Kao *et al* [11] conducted a study where they evaluated the half-time of gastric emptying of liquid meals in patients with moderate to severe TBI, finding that head trauma can cause significantly prolonged gastric emptying [11]. Other studies have shown that TBI can also induce a decrease in both intestinal contractility and transit and an increase in inflammation in intestinal smooth muscle, which may indicate that motility is inhibited in the small intestine due to inflammatory damage secondary to brain injury [10].

On the other hand, delayed gastric emptying has been frequently observed in patients with intracranial hypertension (IH). Increased intracranial pressure (ICP) causes a large increase in sympathetic activity, which is responsible for several of the systemic and peripheral gastrointestinal symptoms [12]; this increase in turn can lead to changes in GI motility and in water and electrolyte absorption. Similarly, Madroszkiewicz *et al* [13] conducted a study to evaluate the effects of acute and chronic ICP on gastric myoelectric activity and found that the most significant changes in gastric activity were

observed in patients after severe traumatic brain injury with acute IH.

PATHOPHYSIOLOGICAL ASPECTS

Under normal conditions, food is liquefied in the stomach by the digestive action of gastric acid and antral contractions [14]. These antral contractions, essential for the crushing of solid food and gastric emptying, are mediated by extrinsic vagal innervation (gastric branches from the anterior and posterior vagal trunks) and intrinsic cholinergic neurons [14,15]. Nitroergic neurons mediate intrinsic inhibitory mechanisms, which facilitate pyloric relaxation and intragastric peristalsis. These neurons are essential for gastrointestinal (GI) muscle relaxation prior to contraction, and are responsible for downstream inhibition prior to upstream contraction, which is induced by excitatory neurons (cholinergic neurons) [14].

These inhibitory and excitatory neuronal effects are transmitted through interstitial cells of Cajal (ICC), fibroblast-like cells (positive for platelet-derived growth factor receptor α - PDGFR α), and smooth muscle cells of GI muscles. This causes the muscular layer of the stomach to behave like a multicellular electrical syncytium so that coordinated contractions, which are initiated in the proximal stomach and involve the entire circumference of the stomach, can propagate into the antropyloric region [14,16,17].

PDGFR α -positive ICCs and fibroblast-like cells are considered to be the pacemaker cells of the gastrointestinal tract and possess the ability to transmit electrical signals (Figure 1) [17]. In gastroparesis, delayed gastric emptying is associated with decreased antral motility and, in some patients, pyloric sphincter dysfunction due to neuromuscular dysfunction [14].

On the other hand, after traumatic brain injury, primary tissue damage (somatic and axonal) induced by mechanical damage to the brain causes the release of intracellular and intraaxonal contents, as well as the extravasation of blood products [18]. In response to this tissue damage, local activation of microglia occurs. At the same time that the local microglial inflammatory response occurs, brain infiltration and accumulation of peripheral immune cells is generated, which enter due to alterations in the blood-brain barrier after TBI [19]. These cells mediate inflammatory processes through the

production of a variety of inflammatory cytokines, chemokines, adhesion molecules, reactive oxygen and nitrogen species, among others [18].

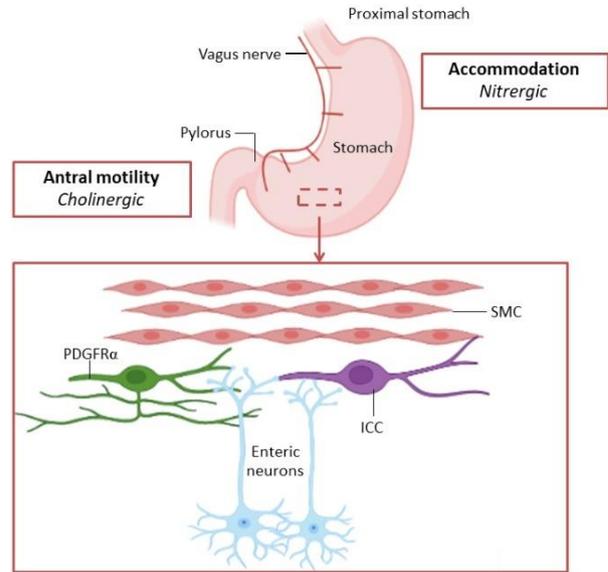


Figure 1. Mechanisms of antral motility, accommodation and gastric emptying. Created by authors with BioRender.

Some studies have shown reductions in the number of ICC in the stomach body of patients with gastroparesis [20,21]. This reduction in ICC could impair conduction of electrical activity through the electrical syncytium and thus interfere with coordinated gastric electrical rhythms, peristalsis and gastric emptying [14]. Both the decrease in the number and damage of ICCs in the stomach of some patients with gastroparesis have been associated with a decrease in the number of M2 anti-inflammatory macrophages, which express the mannose receptor (CD206) and heme oxygenase 1 (HO1) and are responsible for mediating cellular repair. In this way, M2 macrophages protect neural tissue against the effects of oxidative stress and inflammation [14,20].

Thus, a possible explanation for the occurrence of gastroparesis as a complication of an episode of TBI is that a decrease in the number or damage of ICC in patients with a reduced number of M2 anti-inflammatory macrophages would generate a deficiency in the protection of neural tissue against the effects of oxidative stress and inflammation. Ultimately, these events could result in gastric intrinsic neural dysfunction, which would be the cause of gastroparesis

CLINICAL AND DIAGNOSTIC CONSIDERATIONS

GP manifests itself through a wide array of signs and symptoms, including nausea (predominant symptom), vomiting, pain (burning or burning), early satiety, postprandial fullness, abdominal distension, bloating, and upper abdominal discomfort. GP-associated pain is mainly located in the epigastrium, is described as persistent or nocturnal, and is often reported after a meal (food-induced pain) [8,9]. The severity of gastroparesis is assessed by the degree of nutritional impairment or weight loss or by the degree of delayed gastric emptying (e.g., the proportion of food retained in the stomach for a given number of hours), which will be influenced by the method and foods used to test overall stomach function. Similarly, there are several symptom severity scales to assess clinical signs and symptoms [14].

In the neurocritical patient with enteral feeding by nasogastric tube (NGT), increased gastric residuals and intolerance to enteral feeding are typically reported [9]. This delays adequate nutrition, favors aspiration of gastric contents and pneumonias, thus prolonging hospital stay, increasing medical costs and contributing to a higher risk of mortality [4, 6, 9].

DIAGNOSIS

The diagnosis of GP is based on the presence of signs and symptoms and the demonstration of delayed gastric emptying. It should be emphasized that, before assessing gastric motor activity or emptying rate, it is necessary to exclude other possible causes of symptoms. Generally, people in whom GP is suspected require upper endoscopy to exclude mechanical obstruction or ulcer disease. While endoscopy is often normal in patients with delayed gastric emptying, in severe cases, endoscopy may reveal food debris in the stomach, the so-called bezoars. Laboratory tests should rule out water and electrolyte disorders, and glycemia and thyroid function should also be requested. Subsequently, gastric motor function tests can be considered [8,9].

As previously mentioned, documentation of delayed gastric emptying is essential for a definitive diagnosis. The evaluation of gastric emptying includes a variety of methods [22-24]. Currently, scintigraphy is the most widely used diagnostic technique and is considered the gold standard for documenting delayed gastric emptying; using this technique, a radioactive substance is administered

and two-dimensional images show the emitted radiation [7, 24, 25]. Carbon 13 (¹³C)-octanoic acid or ¹³C-acetic acid breath analysis is used in some institutions, but requires more time than the 1- or 2-hour scintigraphy tests [6, 8]. Other diagnostic methods include ultrasound but depend on a specialized operator [6]. When gastric emptying tests are inconclusive, particularly in those patients with pronounced postprandial fullness or early satiety, measurements of gastric accommodation can also be estimated by validated methods such as positron emission tomography (PET/CT) and magnetic resonance imaging (MRI), or by screening tests such as proximal stomach size on gastric scintiscan (taken immediately after ingestion of a radiolabeled meal) or by a water or nutritive drink loading test [26].

In the intensive care setting, the most commonly used method for assessing gastric emptying is the measurement of gastric residual volume (GRV) [24,25], which can be accomplished by connecting a 50 ml syringe to an NGT and aspirating the residual contents. Another way to measure VGR is to connect a drainage bag to the end of an NGT and lower the bag below chest level for 10 minutes [27]. Delayed gastric emptying is often designated when the GRV is 250 ml or more. However, factors such as patient position (low or high elevation from the head of the bed), feeding port tube location (deeper in the body of the stomach or near the gastroesophageal junction), and the internal diameter of the feeding tube (narrow or wide) may affect the GRV [23,24].

THERAPEUTIC APPROACH TO GASTROPARESIS IN THE SETTING OF TBI

The treatment of GP focuses on 2 pillars:

- 1) Restoration of water and electrolyte balance, glycemic control, suspension of drugs that alter gastric motility (pro-gastroparalitics) and modifications in the diet provided, which should be low in volume and lower in calories, but with shorter intervals between servings [28]. Higher kcal and weight meals are associated with longer emptying times. The diet should preferably be liquid and fat-free; fat intake releases cholecystokinin which can further delay gastric emptying. High fiber foods are recommended to prevent the formation of bezoars [6]. In patients with TBI, actual energy needs can be up to 60% higher than expected values [29]. Therefore, it has been emphasized that, in terms of

complications and survival, nutritional support is beneficial for neurocritical patients [30]. Enteral nutrition instead of parenteral nutrition is generally the preferred means of nutritional support. It is indicated for maintaining and restoring electrolyte balance, in addition to providing nutritional [31]. Enteral nutrition can be instituted through many routes, such as NGT and nasoenteric tubes, or by gastrostomy or jejunostomy that simultaneously decompresses the stomach and allows enteral nutrition [32]. Particularly in patients with TBI, GP makes oral nutritional support difficult. To overcome the difficulties associated with GP, transpyloric placement of the feeding tube has been recommended [9, 33]. However, tube displacement and difficulties in passing the tube through the pylorus are common problems. In addition, the need for transpyloric feeding has been questioned, as it does not result in a significant decrease in complications [34]. Therefore, strategies have been developed to improve gastric motility with intragastric enteral feeding.

2) The administration of drugs to stimulate and improve gastric emptying and reduce nausea and vomiting. Several prokinetic agents have been shown to achieve this goal. These drugs increase antral contractility, correct gastric arrhythmias, and improve coordination of antroduodenal movements [6,28]. With recent advances in research on prokinetic agents, the following three categories of drugs are frequently used in GP patients.

Dopamine antagonists: Metoclopramide is a dopamine antagonist with both central and peripheral activity [6]. It acts on dopaminergic (D2) and serotonergic (5-HT3) receptors, and stimulates the release of acetylcholine in myenteric plexus neurons [28]. In addition to its antiemetic effect, it has prokinetic activity [6]. It is more effective in short-term treatments, no longer than 15 days [8]. The usual dose is 10 mg IV 3 or 4 times a day and the dose may be doubled in severe cases. Although frequently used, it may cause neurological symptoms with long-term use [28]. Side effects are related to central dopaminergic blockade causing sporadic acute dystonic reactions, facial spasms, parkinsonian symptoms and asthenia [6, 8, 28]. Domperidone is

another dopamine antagonist, but with peripheral activity only [6]. It has a prokinetic and antiemetic action and has a particularity, it does not cross the blood-brain barrier, therefore, it does not produce extrapyramidal side effects [28]. Superior efficacy and tolerability have been suggested for domperidone over metoclopramide [35, 36]; therefore, it has been considered as the drug of choice. The dose is 10 mg distributed in 4-6 daily intakes [28]. Like metoclopramide, it can produce hyperprolactinemia [6].

Substituted benzamides: Cisapride facilitates acetylcholine release from myenteric plexus neurons through a 5-HT4 receptor-mediated effect [6]. Superior efficacy and tolerability have been suggested for cisapride over metoclopramide [37]. However, due to the increased risk of QT interval prolongation with cardiac arrhythmias, its use in routine clinical practice has been restricted [1]. Cinitapride is another non-antiemetic prokinetic. It is a 5-HT4 receptor agonist. It facilitates the release of acetylcholine. Unlike its predecessor cisapride it does not produce QT interval prolongation or severe cardiac arrhythmias. The usual dose is 1 to 2 mg distributed in two daily doses [28].

Antibiotics: Erythromycin is a macrolide that stimulates gastroduodenal motilin receptors. It is the most potent prokinetic, with a significant improvement in gastric emptying. However, it has no antiemetic action [6]. The dose is 300-750 mg/day distributed in 3-4 intakes, preferably IV [28]. Due to its antibiotic properties, long-term use may lead to the induction of resistant strains. There are other possible side effects such as ototoxicity and pseudomembranous colitis, which limits long-term use in patients with gastroparesis. In addition, the problem of tachyphylaxis makes long-term use less attractive. Concomitant hyperglycemia may interfere with or block its prokinetic property [28].

FUTURE PERSPECTIVES

Traumatic brain injury remains a major cause of mortality, morbidity and economic burden worldwide, and will always be a frequent entity in neurocritical care settings, since its main causes are falls and motor vehicle accidents, which are events that occur on a daily basis in our environment [38,39]. In first world countries, there has been a trend towards reducing TBI incidences driven by

public health interventions such as seat belt legislation, helmet use, and workplace health and safety standards [38]. In underdeveloped countries, as is the case in Latin America, these established prevention standards are not complied with by the majority of their inhabitants, which leads to a higher number of TBI cases in emergency departments. Therefore, the appropriation and acquisition of knowledge on this subject is fundamental.

Knowing the pathophysiological aspects and degrees of severity would help to understand the mechanisms by which different complications occur after TBI, as well as to evaluate the good or bad prognosis of functional recovery and to anticipate the rehabilitation needs of patients.

Gastrointestinal alterations, in this case gastroparesis, as a complication associated with severe TBI is no exception, since there are large gaps in knowledge, its pathophysiology and inconsistencies among published studies on this subject. For this reason, neurogastroenterological research, which aims to improve the understanding of the physiology and pathophysiology of the digestive neurological subsystems from which functional symptoms arise, has aroused great interest within the scientific community. Similarly, research on the relationship between gastroparesis and intracranial hypertension should be expanded, as it has been suggested that correction of these gastric abnormalities may facilitate the recovery of patients with brain lesions.

On the other hand, neuronutrition is also a line of research that has gained strength in recent years, due to the importance of nutrition in patients with neurological disorders; it is necessary for the proper functioning of respiratory muscles, cardiac function, the balance of the coagulation cascade, electrolyte and hormone balance, and renal function, as well as influencing functional recovery and the overall cost of medical care. The need to identify and treat the patient with malnutrition or impaired gastrointestinal function is a critical aspect of patient management [40]. The above explains why research on gastroparesis in the context of TBI is essential to improve specific and overall patient outcomes with general involvement, and thus reduce the rate of secondary complications such as pulmonary aspiration or malnutrition, overall morbidity, mortality, and disability.

CONCLUSION

Traumatic brain injury remains a pathological condition with a considerable burden of disease worldwide. Gastroparesis is a complication that substantially influences morbidity, mortality and disability in the traumatic brain injury patient by intervening in the nutrition process, among many others. Although its pathophysiology is not clearly known, early treatment of its symptoms can substantially improve the prognosis.

REFERENCES

1. Capizzi A, Woo J, Verduzco-Gutierrez M. Traumatic Brain Injury: An Overview of Epidemiology, Pathophysiology, and Medical Management. *Med Clin North Am.* 2020; 104(2):213-238.
2. Traumatic Brain Injury and Concussion. 2021. Available at: https://www.cdc.gov/traumaticbraininjury/get_the_facts.html. Accessed June 21, 2021.
3. Cederberg D, Hansson HA, Visse E, Siesjö P. Antisecretory Factor May Reduce ICP in Severe TBI-A Case Series. *Front Neurol.* 2020; 11:95.
4. Ott L, Young B, Phillips R, McClain C, Adams L, Dempsey R, et al. Altered gastric emptying in the head-injured patient: relationship to feeding intolerance. *J Neurosurg.* 1991; 74(5):738-42.
5. Altmayer T, O'Dell MW, Jones M, Martin V, Hawkins HH. Cisapride as a treatment for gastroparesis in traumatic brain injury. *Arch Phys Med Rehabil.* 1996; 77(10):1093-4.
6. Masaoka T, Tack J. Gastroparesis: current concepts and management. *Gut Liver.* 2009; 3(3):166-73.
7. Stanghellini V, Tack J. Gastroparesis: separate entity or just a part of dyspepsia? *Gut.* 2014; 63(12):1972-8.
8. Parkman HP, Hasler WL, Fisher RS. American Gastroenterological Association Technical review on the diagnosis and treatment of gastroparesis. *Gastroenterology.* 2005; 127(5):1592-622.
9. Frazer C, Hussey L, Bemker M. Gastrointestinal Motility Problems in Critically Ill Patients. *Crit Care Nurs Clin North Am.* 2018; 30(1):109-121.
10. Keshavarzia Z, Afsharic AR, Mohammadzadehd N, Mohebbie M, Mohebbie M, Mollazadeh H. Traumatic Brain Injury and the Gastrointestinal Tract: The Role of Female Sexual Hormones. *J Endocrinol Metab.* 2017; 7(6):163-171.
11. Kao CH, ChangLai SP, Chieng PU, Yen TC. Gastric emptying in head-injured patients. *Am J Gastroenterol.* 1998; 93(7):1108-1112.
12. McAllister TW. Neurobiological consequences of traumatic brain injury. *Dialogues Clin Neurosci.* 2011; 13(3):287-300.
13. Madroszkiewicz D, Thor P, Moskała M, Madroszkiewicz E, Gościński I. Effects of intracranial hypertension on gastric myoelectrical activity evaluated by using clinical and

- radiological symptoms. *Neurol Neurochir Pol.* 2005; 39(1):41-8.
14. Camilleri M, Chedid V, Ford AC, Haruma K, Horowitz M, Jones KL, et al. Gastroparesis. *Nat Rev Dis Primers.* 2018; 4(1):41.
 15. Lucena AF, Tibúrcio RV, Vasconcelos GC, Ximenes JD, Cristino Filho G, Graça RV. Influence of acute brain injuries on gut motility. *Rev Bras Ter Intensiva.* 2011; 23(1):96-103.
 16. Sanders KM, Ward SM, Koh SD. Interstitial cells: regulators of smooth muscle function. *Physiol Rev.* 2014; 94(3):859-907.
 17. Wood JD. Neuropathophysiology of functional gastrointestinal disorders. *World J Gastroenterol.* 2007; 13(9):1313-32.
 18. McGinn MJ, Povlishock JT. Pathophysiology of Traumatic Brain Injury. *Neurosurg Clin N Am.* 2016; 27(4):397-407.
 19. Habgood MD, Bye N, Dziegielewska KM, Ek CJ, Lane MA, Potter A, et al. Changes in blood-brain barrier permeability to large and small molecules following traumatic brain injury in mice. *Eur J Neurosci.* 2007; 25(1):231-8.
 20. Bernard CE, Gibbons SJ, Mann IS, Froschauer L, Parkman HP, Harbison S, et al. Association of low numbers of CD206-positive cells with loss of ICC in the gastric body of patients with diabetic gastroparesis. *Neurogastroenterol Motil.* 2014; 26(9):1275-84.
 21. Stein DM, Feather CB, Napolitano LM. Traumatic Brain Injury Advances. *Crit Care Clin.* 2017; 33(1):1-13.
 22. Nursal TZ, Erdogan B, Noyan T, Cekinmez M, Atalay B, Bilgin N. The effect of metoclopramide on gastric emptying in traumatic brain injury. *J Clin Neurosci.* 2007; 14(4):344-8.
 23. Camilleri M, Parkman HP, Shafi MA, Abell TL, Gerson L; American College of Gastroenterology. Clinical guideline: management of gastroparesis. *Am J Gastroenterol.* 2013; 108(1):18-37; quiz 38.
 24. Kar P, Jones KL, Horowitz M, Chapman MJ, Deane AM. Measurement of gastric emptying in the critically ill. *Clin Nutr.* 2015; 34(4):557-64.
 25. Adike A, Quigley EM. Gastrointestinal motility problems in critical care: a clinical perspective. *J Dig Dis.* 2014; 15(7):335-44.
 26. Orthey P, Yu D, Van Natta ML, Ramsey FV, Diaz JR, Bennett PA, et al. Intra-gastric Meal Distribution During Gastric Emptying Scintigraphy for Assessment of Fundic Accommodation: Correlation with Symptoms of Gastroparesis. *J Nucl Med.* 2018; 59(4):691-697.
 27. Kuppinger DD, Rittler P, Hartl WH, Rüttinger D. Use of gastric residual volume to guide enteral nutrition in critically ill patients: a brief systematic review of clinical studies. *Nutrition.* 2013; 29(9):1075-9.
 28. Godoy D, Panhke P, Piñero G, Videtta W, Aguilera S. Cuidados intensivos en trauma craneoencefálico grave. *Neuroc Colomb.* 2016; 23(3):193-234.
 29. Moore R, Najarian MP, Konvolinka CW. Measured energy expenditure in severe head trauma. *J Trauma.* 1989; 29(12):1633-6.
 30. Hadley MN, Grahm TW, Harrington T, Schiller WR, McDermott MK, Posillico DB. Nutritional support and neurotrauma: a critical review of early nutrition in forty-five acute head injury patients. *Neurosurgery.* 1986; 19(3):367-73.
 31. Pesce M, Borrelli O, Saliakellis E, Thapar N. Gastrointestinal Neuropathies: New Insights and Emerging Therapies. *Gastroenterol Clin North Am.* 2018; 47(4):877-894.
 32. Quigley EM, O'Mahony S, Heetun Z. Motility disorders in the patient with neurologic disease. *Gastroenterol Clin North Am.* 2011; 40(4):741-64.
 33. Thor PJ, Gościński I, Kolasińska-Kloch W, Madroszkiewicz D, Madroszkiewicz E, Furgala A. Gastric myoelectric activity in patients with closed head brain injury. *Med Sci Monit.* 2003; 9(9):CR392-5.
 34. Spain DA, DeWeese RC, Reynolds MA, Richardson JD. Transpyloric passage of feeding tubes in patients with head injuries does not decrease complications. *J Trauma.* 1995; 39(6):1100-2.
 35. Dumitrascu DL, Weinbeck M. Domperidone versus metoclopramide in the treatment of diabetic gastroparesis. *Am J Gastroenterol.* 2000; 95(1):316-7.
 36. Patterson D, Abell T, Rothstein R, Koch K, Barnett J. A double-blind multicenter comparison of domperidone and metoclopramide in the treatment of diabetic patients with symptoms of gastroparesis. *Am J Gastroenterol.* 1999; 94:1230-1234.
 37. Feldman M, Smith HJ. Effect of cisapride on gastric emptying of indigestible solids in patients with gastroparesis diabetorum: a comparison with metoclopramide and placebo. *Gastroenterology.* 1987; 92:171-174.
 38. Khellaf A, Khan DZ, Helmy A. Recent advances in traumatic brain injury. *J Neurol.* 2019; 266(11):2878-2889.
 39. Suchner U, Senftleben U, Eckart T, Scholz MR, Beck K, Murr R, et al. Enteral versus parenteral nutrition: Effects on gastrointestinal function and metabolism. *Nutrition.* 1996; 12:13-22.
 40. Slone DS. Nutritional support of the critically ill and injured patient. *Crit Care Clin.* 2004; 20(1):135-57.