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## Influence of acute brain injuries on gut motility

### *Lesões cerebrais agudas e sua influência sobre a motilidade gastrointestinal*

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#### ABSTRACT

Subarachnoid hemorrhage can increase intracranial pressure, causing significant morbidity. Acute gastric dilation and delayed gastric emptying are commonly seen in patients with intracranial hypertension, and correction of these gastric abnormalities can facilitate the recovery of patients with brain injuries. We conducted a literature review of both national and international health sciences medical journals and electronic libraries spanning the last twenty-eight years and focused on the brain, gut motility and gastric emptying functional axis either in experimental animal models of brain injury or patients with acute cerebral injuries. Decreased parasympathetic tonus is a potential cause of intracranial hypertension-related food intolerance. Changes in gastrointestinal transit after a brain injury follow a biphasic pattern: an initial phase of ac-

celerated gastric emptying and a late stage of intestinal lethargy. Changes in the physiology underlying gut motility may be essential for homeostatic stabilization in hemodynamically unstable patients. Research studies are necessary to understand the difficult management of intensive care patients with intracranial hypertension secondary to subarachnoid hemorrhages resulting from traumatic brain injuries or rupture of a cerebral aneurysm. Increased intracranial pressure induces massive increases in sympathetic activity, which is responsible for many of the peripheral systemic and gastrointestinal symptoms. Brain injuries leading to significant increases in intracranial pressure result in delayed gastrointestinal emptying due to autonomic nervous system changes.

**Keywords:** Brain/ injury; Intracranial hypertension/etiology; Gastric emptying; Gastrointestinal motility

#### INTRODUCTION

Cerebral parenchyma (80% of the total volume), cerebrospinal fluid (CSF) (10%) and blood (10%) are contained within a rigid and constant volume compartment (the skull). Any volume change involving one of these components will be compensated by adaptive changes in the volume of the remaining components. When the compensatory mechanisms are exhausted, intracranial hypertension (ICH) ensues and is characterized by increased intracranial pressure (ICP) above 20 mmHg. Acute ICH may be caused by head trauma associated with hematomas, stroke, cerebral aneurysm, subarachnoid hemorrhage (SAH) and other causes.<sup>(1)</sup>

Increased ICP may cause changes in gastrointestinal motility as well as water and electrolyte absorption. Studies have evaluated different

means of food administration to brain injury patients as tool to reduce gastrointestinal symptoms. Of note, food intolerance may be associated with increased morbidity and increased hospital stay costs.<sup>(2,3)</sup>

Considering the paucity of both national and international studies correlating SAH, ICH and gastric emptying (GE), the main objective of this paper is to compare and discuss physiological and pathophysiological related to SAH, ICH and gut motility.

## METHODS

A literature search was conducted to analyze the pattern of gut motility following acute brain injury with ICH. Articles discussing possible therapeutic approaches for ICH-related gut complications were also evaluated. The literature search included national and international health sciences journals, and we searched for articles related to the brain-gastrointestinal tract functional axis and its behavior either in experimental animal models of brain injury or acute brain injury patients. Using the inclusion criteria, a web based search was conducted on the following electronic libraries: Scientific Electronic Library Online (SciELO)<sup>®</sup>, Periódicos/Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES)<sup>®</sup>, PubMed/Medline<sup>®</sup> and Google Scholar Beta<sup>®</sup>.

Twenty-five articles published between 1982 and 2010 were selected. Of those, eleven focused on the influence of ICH on gut motility (GM), ten discussed means of nutrition of administration in moderate to severe head trauma (HT) (Glasgow coma scale < 8), and finally, four articles discussed the main metabolic changes in head trauma subjects, with an emphasis on nutritional support.

### **Influence of intracranial hypertension on gut motility**

Eleven articles about ICH influence about gut motility were analyzed. Five (45.4%) were related to gastric and intestinal emptying, four (36.3%) focused on pressure changes throughout the gastrointestinal tract (GIT) (two studied the amplitude and frequency of food propellant contractions, and the other two analyzed the inferior esophageal sphincter behavior under ICH conditions), and two (18.1%) studies evaluated GIT electrical activity, studying the migratory myoelectric complex by means of body surface electrodes or electrogastrogram. Of all of the

articles, two (18.8%) reported that HIC variation is directly proportional to gastric contraction intensity, based on a GE analysis of the amplitude and frequency of contractions in anesthetized rats with intra-cerebral cannulation-induced ICH. The remaining nine (81.8%) articles found that increased ICP is related to slower GIT transit, and this food bolus transit delay is associated with intolerance to enteral nutrition. Pharmacological intervention to accelerate the GIT was evaluated in one of the analyzed articles. Another study was designed to evaluate the association between ICP changes in thirty-seven intracranial tumor patients who performed Valsalva's maneuver during evacuation. All patients performed the maneuver, independent of constipation, and no increased ICP decompensation was observed. Additional studies details are displayed on chart 1.

### **Forms of nutrition and means of administration in moderate to severe HT patients**

Ten studies analyzing the best forms of nutrition for HT patients were evaluated. Five (50%) assessed the best ways to deliver nutrition to these patients, two (20%) analyzed nutrition progression in the days following the HT, two (20%) evaluated the benefits of enteral versus parenteral nutrition, and one (10%) discussed tolerance of enteral nutrition. Regarding the means of administration, nasogastric (NG) and nasojejunal (NJ) tubes were compared. One of the articles concluded that the best caloric supply, nitrogen balance and nitrogen consumption were achieved with an NJ tube, and this was also associated with less infections and shorter lengths of stay. Another article concluded that patients develop moderate food intolerance when fed proximal to the ligament of Treitz, as shown by a better tolerance achieved by the group of patients fed distal to this ligament. Endoscopic percutaneous feeding, evaluated by one article, showed good nutritional support. Continuously administered food was better tolerated than bolus administration. Two of the analyzed studies agreed that prokinetic agents are ineffective for patients receiving enteral nutrition.

Regarding nutrition progression, six months was established by one of the articles as the time when the patient returns to normal eating habits, but most patients in this study showed signs of malnutrition. Early nutrition support was related to lower mortality rates.

Parenteral nutrition was shown to be more

**Chart 1 – Influence of intracranial hypertension on gut motility**

References	Study	Method	Results	Conclusion
Thor et al. 2003 <sup>(7)</sup>	Clinical trial	Gastric myoelectric activity analysis in 24 HT patients.	Electrogastrograms showed bradygastria in 9.7%; normogastria in 88.3%; and tachygastria in 2%. The sign amplitude was increased relative to the control group.	Severe head trauma patients have gastric dysrhythmias and food intolerance.
Kacker, Mehta, Gupta 1999 <sup>(20)</sup>	Experimental	ICH induced with saline intracerebral ventricular injection for gastric residue evaluation. Pharmacologic intervention modulation was evaluated.	Higher ICH was associated with increased gastric retention. Clonidine, prazosin or ondansetron failed to change the GE. Cisapride caused a partial reversal, and low-dose carbachol showed better reversal than high-dose carbachol.	The protective effects of cisapride and carbachol suggest that vagal activity suppression from increased ICP may inhibit GE.
Torres, Diccini 2006 <sup>(6)</sup>	Cohort	Evaluation of constipation and Valsalva's maneuver in intracranial tumor patients with ICH	A total of 16.2% had constipation. No ICH decompensation from Valsalva's maneuver was observed.	Although intestinal behavior is influenced by ICH, constipation has no influence on increased ICH.
Ott et al. 1991 <sup>(13)</sup>	Cohort	Evaluation of enteral nutrition intolerance, based on GE, in HT patients.	First week from trauma: biphasic response. Second week: some with biphasic response. Third week: GE accelerated in 100%.	GE changes may affect enteral nutrition tolerance.
Livingston et al. 1991 <sup>(37)</sup>	Experimental	Evaluation of the amplitude and frequency of gastric contractions after ICH.	Increased amplitudes, without frequency changes. Vagotomy blocked gastric contractility increase.	An increase in ICP increases the strength of gastric contractions.
Garrick et al. 1988 <sup>(10)</sup>	Experimental	Evaluation of gastric antrum and duodenum contractions in rabbits with induced ICH.	An ICP increase to 13 cm H <sub>2</sub> O suppressed gastric and duodenal contractility. After ICP normalization, contractility returned to normal.	An ICP increase quickly and reversibly inhibits gastric and duodenal motility.
Matthews et al. 1988 <sup>(8)</sup>	Experimental	Migratory myoelectric complex (MMC) evaluation in ICH cats.	The periodicity and shapes of gastro-esophageal waves became irregular. MMC did not change in the antrum or pre-pylorus.	ICH leads to consistent and reproducible MMC changes.
Kao et al. 1998 <sup>(38)</sup>	Clinical trial	GE time was evaluated in 3 HT patients	A total of 80% of the patients had prolonged GE time.	HT patients have prolonged periods of GE with liquid meals.
Shteyer et al. 1998 <sup>(39)</sup>	Clinical trial	Esophageal pH monitoring in hydrocephalus children.	Gastro-esophageal reflux was reduced in 100% of children after ventriculo-peritoneal derivation.	An ICP increase inhibits lower esophageal sphincter pressure, causing reflux.
Vane et al. 1982 <sup>(40)</sup>	Experimental	Lower esophageal sphincter pressure evaluation in post-HT patients.	Lower esophageal sphincter pressure, as measured with transducers, was reduced in all post-HT patients.	An ICP increase leads to lower esophageal sphincter pressure reduction.
Cristino-Filho et al. 2009 <sup>(41)</sup>	Experimental	Analysis of the influence of ICH on rats gastric tonus.	Gastric volume was reduced by 14.0%, 24.5% and 30.6% following an ICP increase to 20, 40 and 60 mmHg, respectively.	ICH reduces the gastric volume by increasing gastric tonus in anesthetized rats.

HT – head trauma; GE – gastric emptying; ICH – intracranial hypertension; ICP – intracranial pressure; MMC – myoelectric migratory potential.

beneficial than enteral nutrition for post-HT patients, as it did not interfere with either conventional ICH control therapy or incremental ICP in most of the patients. Another comparative trial reported a 44.4% death rate among patients receiving enteral nutrition, compared with no deaths among those receiving parenteral nutrition during the hospital rehabilitation phase. Enteral nutrition tolerance was inversely proportional to ICP and injury severity. Chart 2 summarizes the ten evaluated articles.

### Metabolic changes in head injury subjects

All of the four analyzed articles (100%) considered appropriate nutrition fundamental for meeting post-trauma ICH hypermetabolism requirements, for better clinical outcomes and for reducing the morbidity and mortality of patients. Independent of the food intolerance developed by most of enteral nutrition patients, there was a consensus among all articles that failing to supply metabolic requirements is an important predictor of mortality. However, in

**Chart 2 – Means of administering enteral nutrition to head trauma patients**

References	Study	Method	Results	Conclusion
Klodell et al. 2000 <sup>(42)</sup>	Clinical trial	A total of 118 patients with HT were evaluated for nutrition given by percutaneous gastrostomy.	Intra-gastric feeding was well tolerated by 97% of the patients; 4% had gastric contents aspiration.	No evidence of food intolerance was found for percutaneous gastrostomy enteral nutrition.
Young et al. 1987 <sup>(31)</sup>	Clinical trial	Evaluation of the influence of enteral and parenteral nutrition on the treatment of HT patients.	Conventional therapy for ICH control failed to control ICP in 36% of patients with parenteral nutrition and 38% of patients with enteral nutrition.	Parenteral nutrition had better results and may be given without influencing either ICH or the therapies used.
Rapp et al. 1983 <sup>(2)</sup>	Clinical trial	Analysis of the effect of parenteral and enteral nutrition in 39 post-HT patients.	A total of 44.4% of the enteral nutrition patients died; no parenteral nutrition patient died during the rehabilitation phase.	Parenteral nutrition renders the nitrogen balance more positive, increases serum albumin levels and increases lymphocytes counts.
Härtl et al. 2008 <sup>(3)</sup>	Cohort	Nutrition start and energy supply were evaluated in 797 deaths due to HT.	Nutrition that started 5 to 7 days after HT was associated with a 2- to 4-fold increased risk of death. Every reduction of 10 kcal/kg increased the death rate by 30-40%.	Good nutrition support up to 5 days after HT reduced mortality by 2 deaths/week.
Graham et al. 1989 <sup>(43)</sup>	Cohort	NJ tube and NG tube feeding was evaluated in HT patients.	NJ tube nutrition showed lower infection rates and shorter hospital stays.	HT patients tolerate jejunal hyper-nutrition, although with reduced hydroaerial sounds.
Krakau et al. 2007 <sup>(44)</sup>	Case control	Analysis of nutrition in the medical charts of patients within 6 months from HT.	A total of 92% were fed orally; 84% were independently nourished; and 66% had signs of malnutrition.	HT patients usually achieve nutrition independence 6 months after trauma.
Rhoney et al. 2002 <sup>(4)</sup>	Cohort	GE evaluation in HT patients with either continuous or bolus nutrition administration.	Food intolerance was more frequent in the bolus feeding group. Prokinetics failed to reduce GE time.	Continued feeding is better tolerated in ICH patients. Prokinetics are not beneficial.
Kozar et al. 2002 <sup>(45)</sup>	Clinical trial	Evaluation of vomiting, abdominal distension and diarrhea in HT patients.	Patients fed proximally to the ligament of Treitz showed more food intolerance.	Food intolerance may be reduced by feeding distal to the ligament of Treitz.
Bochicchio et al. 2006 <sup>(46)</sup>	Cohort	Tolerance to NG tube nutrition was evaluated in HT patients.	A total of 100% of patients had gastric residues up to 48 hours after trauma. Prokinetic agents failed to show benefits.	Patients with barbiturate-induced coma develop paralytic ileus.
Norton et al. 1988 <sup>(35)</sup>	Cohort	Enteral nutrition tolerance was evaluated in HT patients.	Enteral nutrition tolerance was inversely proportional to ICP and injury severity.	Poor enteral nutrition tolerance persists for about 14 days after brain injury.

HT – head trauma; ICH – intracranial hypertension; ICP – intracranial pressure; NG tube – nasogastric tube; NJ tube – nasojejunal tube.

one of the articles, excessive caloric support during the first days after a brain injury was associated with additional stress.

### PHYSIOLOGY AND PATHOPHYSIOLOGY OF THE INFLUENCE OF THE AUTONOMIC NERVOUS SYSTEM (ANS) ON GUT MOTILITY

SAH is an example of an injury that causes an increase in ICP, resulting in high morbidity levels. It is caused mainly by traumatic brain injuries and is seen in up to 59% of severe HT cases. SAH is a poor prognosis indicator in HT patients, especially when the Glasgow coma scale rating is less than or equal to thirteen. Ideal treatment of these patients is based on intensive neurological measures. GIT changes in patients with altered consciousness levels may involve emesis and aspiration of gastric contents to the trachea and bronchial tree, with increased morbidity.<sup>(4-8)</sup> Acute gastric dilation and delayed GE are relevant pathophysiological changes in ICH patients, and normalization of these disturbances is useful for effective clinical management. However, the mechanisms of gastrointestinal changes in human ICH patients are still poorly understood.<sup>(9-12)</sup>

GE is modulated by ANS action. Gut motility disorders in HT patients may be directly caused by the trauma mechanics or may be due to neural injury or changes in the release of mediators. ICH leads to a biphasic systemic autonomous stimulation. It results from hyperactivity of the parasympathetic and sympathetic systems at different times.<sup>(13)</sup> Recent experimental trials have shown secondary abnormal autonomic responses in patients with increased ICP, with fast GE during the initial phase and delayed gastric transit in a later phase.<sup>(13)</sup>

The parasympathetic system is known to modulate GIT activity, regulating both its motility and hydroelectrolytic dynamics. During deglutition, the proximal region of the stomach relaxes in conjunction with the inferior esophageal sphincter.<sup>(14)</sup> Intraluminal pressure drops in both regions before the food bolus arrives due to smooth muscle relaxation in these regions. Next, stomach pressures gradually return to previous levels. Therefore, large volumes of food may be ingested and stay in the stomach with minimal intra-gastric pressure increase. For instance, the human stomach is able to receive 1,600 mL of air with a 10 mmHg pressure increase.<sup>(15)</sup> Receptive relaxation is mediated by a neural reflex involving

both afferent and efferent vagus nerve pathways. When this nerve is transected, receptive relaxation is abolished, the stomach becomes less distensible, and the gastric contractility increase seen with increased ICP is blocked.<sup>(16)</sup>

### ANS modulation and pharmacological basis for GIT autonomic dysregulation therapy

Based on the physiology of ANS and GIT interactions, several pharmacological trials were conducted to establish the actual pathophysiological role of the ANS on GIT changes following brain injury with ICH. Cisapride is an effective prokinetic agent that has been clinically approved for use in reflux esophagitis, gastroparesis and dyspepsia. Cisapride is believed to work by increasing cholinergic activity mediated by 5-HT<sub>4</sub> receptors. Cisapride can partially revert ICH-induced inhibition of GE.<sup>(17-19)</sup> Carbachol, a muscarinic acetylcholine receptor inhibitor, reverted the ICP increase-induced GE inhibition. However, this study reported better protection with lower carbachol doses, which was a peculiar finding. It is likely that the augmented autonomic ganglia nicotinic activity induced by higher carbachol doses could partially suppress the gastric prokinetic effects of the drug.<sup>(20)</sup>

Data on sympathetic and parasympathetic activity modulation indicate that changes in the activity of these systems may play an important pathophysiologic role in ICH-induced GE inhibition. Support of cholinergic activity may be useful to normalize this inhibitory effect.<sup>(20)</sup> Sympathetic nerves have adrenergic efferent fibers to the stomach, which inhibit gastric motility and are mediated by  $\alpha$ -adrenergic pre-synaptic receptors present in intramural cholinergic neurons.<sup>(21,22)</sup> Alpha-adrenergic receptors were found centrally in the triggering chemoreceptor zone, and blockade of these receptors appears to prevent noradrenalin-induced emesis.<sup>(23)</sup> Increased ICP leads to activation of medullary centers, primarily by pressure transmission to the brain troncus or secondarily by hypothalamic activation of descending modulatory pathways. Active descending discharge in turn leads to a systemic hyper-adrenergic response, including the splanchnic sympathetic pathway.<sup>(24)</sup> How this sympathetic activation is able to act on gastric motility and gastric complacency (GC) is still under discussion and requires additional studies. Animals that underwent splanchnicectomy and celiac

gangliectomy had no changes in gastric volume (GV) upon ICP increase, suggesting that the ICP-induced stomach tonus increase phenomenon is mediated by a splanchnic pathway.<sup>(25)</sup>

Prazosin, a type  $\alpha$ 1 adrenergic inhibitor, reduces vomiting after ICP increase. This was seen following both peripheral and central dosing of the drug, although the best effects were seen with intra-ventricular brain administration.<sup>(26)</sup> Since then, many emesis-causing stimuli have been shown to delay GE. Therefore, the effects of prazosin on ICP-induced GE inhibition were investigated, given its effectiveness against vomiting induced by the same stimuli. However, both centrally and peripherally administered prazosin failed to improve ICH-induced GE inhibition.<sup>(26)</sup> In contrast, specific noradrenergic blocking drugs lead to a partial reversion of ICP-induced GE inhibition. Prazosin was ineffective in increasing GE, suggesting that increased sympathetic activity may be responsible for GE inhibition.<sup>(26)</sup>

Clonidine, an  $\alpha$ 2-adrenergic agonist, inhibits gastrointestinal transit following both central and peripheral administration, and this effect is mediated by the vagus. However, it failed to affect ICP-induced GE inhibition, either because the ICP-induced sympathetic discharge was insufficient or because the clonidine effect, mediated by the vagus nerve, was antagonized.<sup>(27,28)</sup>

## NUTRITION SUPPORT FOR ACUTE BRAIN INJURY PATIENTS

These GIT changes in severe brain injury patients led us to discuss the use of artificial nutrition for patients with increased ICP. The hypermetabolism and hyper-catabolism of these patients require higher nutritional supplies.<sup>(29)</sup> Infection is common and prolongs the recovery time.<sup>(30)</sup> Therefore, appropriate nutrition support may reduce susceptibility to sepsis and increase immunocompetence.<sup>(2,31)</sup> Acute gastric dilation and delayed GE may be pathophysiologically relevant for HT patients. Normalization of these factors may be useful for central nervous system (CNS) injury patients.<sup>(9)</sup>

An important article evaluated the nutrition of patients with severe HT and analyzed the time of beginning enteral nutrition and the calories supplied. The probability of survival increased when enteral nutrition was started earlier and with higher caloric supplies. Mortality was two- and four-fold higher

among patients for whom enteral nutrition was not started within the first 5 and 7 days after HT, respectively. It should be highlighted that a minimum of 25 kcal/kg/day was associated with improved prognosis.<sup>(3)</sup>

Early nutrition support via parenteral nutrition is more effective than enteral nutrition for supplying energy, proteins and fluids after neurological injury.<sup>(32-34)</sup> However, enteral nutrition has been reported to be more beneficial than parenteral nutrition, given its lower cost, lower infection risk, protection of intestinal epithelium integrity, improvement of immunocompetence and attenuation of the metabolic stress response during the illness critical phase.<sup>(35)</sup> Some severe HT patients, however, cannot tolerate enteral nutrition and show increased gastric residues, prolonged paralytic ileus, abdominal distension and diarrhea.<sup>(35)</sup> In this clinical condition, enteral nutrition success appears to be inversely correlated with the ICP and trauma severity. The mechanism of this relationship may be multi-factorial. Hypoalbuminemia is another cause of unsuccessful enteral nutrition found in HT patients. In this condition, enteral absorption ability is impaired, as albumin is responsible for maintaining GIT oncotic pressure.<sup>(36)</sup>

Increases in ICP as a result of SAH induce massive increases in sympathetic activity, which is responsible for several peripheral symptoms as a response to changes in the brain.<sup>(11)</sup> This emphasizes the pathophysiological influence of sympathetic stimulation via its gastric motility inhibitory effect and the ability of ICH to change gastrointestinal dynamics, including its motility and hydroelectrolytic absorption. It should be emphasized that these GIT changes may be essential for homeostatic stabilization in conditions of hemodynamic instability. Volume restitution and immediate survival upon bleeding in monogastric animals, such as rats and rabbits, are impaired in previously enterectomized or fasting animals.<sup>(36)</sup> Observations of model animals are key to understanding the difficulties in managing nutrition and blood volume in intensive care patients progressing with secondary ICH following severe HT.<sup>(36)</sup>

## CLOSING REMARKS

ICH is a complex SNC injury phenomenon that has two different phases, which are influenced by autonomous stimulation. Most of the contemporary trials analyzed in this review support the double

SNC stimulation theory.

Early enteral nutrition in patients with severe HT is important for managing the care of polytrauma patients. However, achieving adequate energy supply in this way may be challenging in neurological injury patients, since delayed GE is a common clinical contraindication for enteral feeding. In these cases, parenteral nutrition should be considered. Therefore, the ICP level at which a hypercatabolic patient can be safely fed via enteral nutrition should be established because this method supports GIT transit, nutrient absorption and more effective recovery.

## RESUMO

A hemorragia subaracnóide é um exemplo de agravo capaz de elevar a pressão intracraniana a patamares de expressiva morbidade. A dilatação gástrica aguda e o retardo do esvaziamento gástrico são alterações de relevância fisiopatológica em pacientes com hipertensão intracraniana, sendo a normalização desses parâmetros útil para otimizar a recuperação dos pacientes vítimas de lesões do sistema nervoso central. Conduziu-se uma revisão bibliográfica em revistas

de pesquisa médico-acadêmica e bibliotecas eletrônicas na área das ciências da saúde nacionais e internacionais nos últimos vinte e oito anos a respeito do eixo funcional cérebro-trato gastrointestinal e seu comportamento em animais experimentais ou pacientes com lesão cerebral aguda. A diminuição do tônus parassimpático é uma potencial causa da intolerância alimentar associado a hipertensão intracraniana. O comportamento do esvaziamento gástrico e do trânsito do trato gastrointestinal seguem padrão bifásico: uma fase inicial de esvaziamento gástrico acelerado e uma fase tardia de letargia intestinal. Observações experimentais são importantes para compreender o difícil manejo nutricional e volêmico de pacientes em terapia intensiva que evoluem com HIC secundária a um trauma crânio encefálico ou após hemorragia subaracnóide pós-rotura aneurismática cerebral. A elevação da pressão intracraniana causa incremento na atividade simpática, que é responsável por muitos dos sintomas periféricos sistêmicos e gastrintestinais. Conclui-se que as lesões cerebrais agudas que cursam com elevação importante da pressão intracraniana retardam o esvaziamento gastrointestinal tendo como via fisiopatológica as alterações no sistema nervoso autônomo.

**Descritores:** Encéfalo/lesões; Hipertensão intracraniana/etiologia; Esvaziamento gástrico; Motilidade gástrica

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