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Clinical significance of gastric dysrhythmias

Chung Ouyang

Chung Ouyang, MD, Division of Gastroenterology. Department of Internal Medicine. Medical Center. The University of Michigan. United States

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GASTRIC DYSRHYTHMIAS

Physiologic role of the gastric slow wave[1,2]

As in the heart, the stomach possesses pacemaker tissue in the gastric body which generates an oscillation of the gastric membrane potential known as the pacesetter potential or slow wave. In man, the gastric slow wave oscillated at 3 cycles per minute (cpm).

The slow wave occurs with nearly constant frequency and is present continuously regardless of the contractile state of the stomach. In the noncontracting state, the slow wave amplitude is not of sufficient magnitude to reach the threshold depolarization necessary to induce contraction. If the stomach receives a neural or humoral stimulus, the plateau potential is enhanced and/or action potential s are generated which increase the level of depolarization about the mechanical threshold and the gastric smooth muscle contracts. Because the critical level of depolarization is reached only during the plateau phase of each slow wave, the maximal number of gastric contractions is determined by the slow wave frequency.

Patterns of gastric dysrhythmias[3]

Human tachygastria is defined as the presence of a slow wave frequency greater than 4.5 cpm for more than 60 s. Tachygastria is associated with decreased contractile activity; This is because tachygastric signals are of such low amplitude that neurohumoral input cannot provide the depolarization necessary to reach the contractile threshold.

Most tachygastrias originated in the antrum, assume the role of the dominant pacemaker, and entrain the rest of the antrum and body to the higher frequency. Thus tachygastric slow waves often propagate in a retrograde direction.

Spontaneous episodes of abnormally slow electrical oscillations, termed bradygastria, have been noted infrequently in healthy humans. Bradygastria, defined as the presence of a slow wave frequency less than 2 cpm for at least 1 min, usually originated in the body of the stomach and propagates in the normal antegrade direction. Because of the reduced frequency of slow wave activity, bradygastria results in a diminution of gastric contractile activity.

A third rhythm disturbance, termed mixed gastric arrhythmia, consists of bursts of alternating slow and rapid slow wave activity in a manner analogous to the sick sinus syndrome of the heart. Mixed arrhythmias have features of both tachygastria and bradygastria.

Abnormalities of the gastric slow wave frequency (tachygastria, bradygastria, mixed arrhythmia) may spontaneously occur which are associated with disturbances in normal gastric contractile activity.

Mechanisms of formation of gastric dysrhythmias[4-6]

The mechanisms responsible for generation of gastric dysrhythmias are unknown but may involve neural factors and local condition within the gastric smooth muscle wall. The causes of gastric dysrhythmias are probably different from cardiac arrhythmias as most cardiac antiarrhythmic drugs do not prevent gastric slow wave disturbances.

Tachygastria can be induced by activation of neural pathways. The best model for this is circular vection, in which a subject placed within a revolving drum experiences a sensation of selfrotation and motion sickness. This experimental motion sickness is associated with release of catecholamine and β-endorphin and is blocked by atropine suggesting the involvement of adrenergic, opiate, and cholinergic neural pathways.

Several hormones can modify the slow wave frequency in canine and human models. Intravenous metenkephalin and β-endorphin induce tachygastria, bradygastria, and mixed arrhythmias in dogs. Similarly gastric dysrhythmic capabilities have been demonstrated for insulin, secretin, cholecystokinin, pentagastrin, glucagon, and somatostatin. Dysrhythmias resulting from these hormones exhibit characteristics very similar to spontaneous slow wave disturbances suggesting possible roles as physiologic mediators.

Prostaglandin E_2 induces both tachygastria and bradygastria in dogs. In isolated gastric muscle, prostaglandin E_2 increases the spontaneous electrical frequency, with shortening and reduction of the amplitude of the plateau potential, whereas the prostaglandin synthesis inhibitor, indomethacin, decreases the slow wave frequency with plateau potential enhancement, suggesting that endogenous prostaglandins act as physiologic accelerants of the gastric slow wave.

Indomethacin prevents dysrhythmias induced by met-enkephalin in dogs. In gastric smooth muscle tissue from a patient who underwent antrectomy for gastroparesis, indomethacin reduced the electrical cycling rate from 9 cpm to 3 cpm, which was associated with prolongation of the plateau potential and increased contractile

Table 1 Effects of medications on gastric emptying

Delays Gastric Emptying
Alcohol (high concentration)
Aluminum hydroxid antacids
Atropine
Beta agonist
Calcitonin
Calcium channel blockers
Dexfenfluramine
Diphenhydramine
Glucagon
Interleukin-1
L-dopa
Lithium
Omeprazole
Ondansetron
Opiates
Phenothiazine
Propantheline bromide
Sucralfate
Tetrahydrocannabinol
Tobacco
Tricyclic antidepressants
Accelerates gastric emptying
Beta blockers
Cisapride
Diazepam
Domperidone
Histamine H_2 antagonist
Metoclopramide
Naloxone
Prostaglandin E_2

Table 2 Drugs with prokinetic properties on the stomach

Medication	Mechanism(s) of Action	Dosing
Metoclopramide	Dopamine receptor antagonism Stimulate acetylcholine release from enteric nerves 5HT$_3$ receptor antagonism	5-20 qid
Cisapride	Stimulate acetylcholine release from enteric nerves Direct stimulant of smooth muscle contraction receptor 5HT$_3$ antagonist	5-20 mg tid to qid
Erythromycin	Motilin receptor agonist	50-200 mg qid
Domperidone	Peripheral dopamine receptor antagonist (Does not cross blood brain barrier)	10-30 mg qid
Bethanechol	Muscarinic receptor agonist	25 mg qid

activity. These studies suggest a role for endogenous prostaglandins in both pharmacologically-induced and spontaneous gastric dysrhythmias.

Clinical conditions associated with gastric dysrhythmias[7-9]

In healthy individuals, the incidence of tachygastria, bradygastria, or mixed arrhythmia is extremely low, however several clinical syndromes have been shown to be associated with an increased frequency of gastric dysrhythmias.

The presence of gastric dysrhythmias with these syndromes is associated with nausea and vomiting and, in many instances, with delays in gastric emptying as demonstrated by radionuclide gastric emptying scans.

In diabetic gastroparesis, 9 of 10 patients in one study had tachygastria whereas a second study of 6 patients reported 1 with tachygastria, 2 with bradygastria, and 3 with a flatline EGG pattern. Other investigatorshave documented normal slow wave frequencies in diabetics with gastroparesis; However in these patients the normal increase in EGG signal amplitude after meal ingestion was not seen. Thus several different slow wave disturbances may be found in diabetes. The slow wave disturbances found in diabetic gastroparesis may be mimicked by induction of acute hyperglycemia in

Table 3 Clinical conditions associated with the development of gastric slow wave dysrhythmias

Diabetic gastroparesis
Idiopathic gastroparesis
Nonulcer dyspepsia
Unexplained nausea and vomiting
Nausea of the first trimester of pregnancy
Motion sickness Anorexia nervosa
Gastric ischemia
Gastroparesis associated with abdominal malignancy

healthy volunteers suggesting that elevated plasma glucose by itself may be disruptive to slow wave rhythmicity.

The other major groups of individuals to be evaluated with EGG are those with unexplained nausea and vomiting and those with idiopathic gastroparesis. Nine of 14 patients with unexplained nausea in one study had runs of tachygastria or mixed arrhythmia. A larger study compared EGG findings in 48 patients with idiopathic nausea with 52 healthy volunteers. Twenty-three of the 48 patients had either mixed arrhythmias, tachygastria, or loss of the physiologic increase in signal amplitude after a meal whereas none of the healthy volunteers exhibits abnormalities. The loss of the signal amplitude increase after a meal correlate d with delays in gastric emptying in these patients.

The source of the abnormality causing slow wave disturbances in idiopathic gastroparesis is unknown. A microscopic analysis of the gastric wall from a 5 mo old child with unexplained gastric retention revealed no abnormalities in the smooth muscle or myenteric plexus, but electrophysiologic studies showed reduction of plateau potential duration and amplitude.

Other clinical conditions associated with gastric dysrhythmia include the nausea of the first trimester of pregnancy, anorexia nervosa, motion sickness, and is chemic gastroparesis. The gastric dysrhythmias noted during pregnancy may be reproduced by administration of progesterone with or without estradiol suggesting a hormonal etiology of the slow wave disturbances.

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