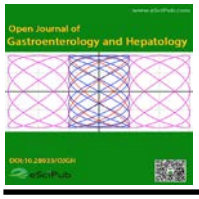
Review Article **OJGH (2019) 2:9**



Open Journal of Gastroenterology and Hepatology
(ISSN:2637-4986)

Domination of Gastric Complications Among Diabetic Patients

Abdul Kader Mohiuddin

Department of Pharmacy, World University of Bangladesh, 151/8, Green Road, Dhanmondi, Dhaka – 1205, Bangladesh

ABSTRACT

This article covers the epidemiology, pathophysiology/complications and management of diabetic gastroparesis (DGP), and more broadly diabetic gastroenteropathy, which encompasses all the gastrointestinal manifestations of diabetes mellitus (DM). Hyperglycemia, autonomic neuropathy, and enteric neuromuscular inflammation and injury are implicated in the pathogenesis of delayed gastric emptying (GE). Initial options include dietary modifications, supplemental oral nutrition, and antiemetic and prokinetic medications. Patients with more severe symptoms may require a venting gastrostomy or jejunostomy and/or gastric electrical stimulation (GES). To date, few population-based studies have estimated the true prevalence and incidence of gastroparesis. Nonetheless, its prevalence appears to be rising, as does its incidence among minority populations, documented via hospitalizations, which can impose significant economic burdens on patients.

Keywords: gastroparesis; pyloric dysfunction; diabetes; delayed gastric emptying; dyspepsia; gastric electrical stimulation

***Correspondence to Author:**
Abdul Kader Mohiuddin
Department of Pharmacy, World University of Bangladesh, 151/8, Green Road, Dhanmondi, Dhaka – 1205, Bangladesh

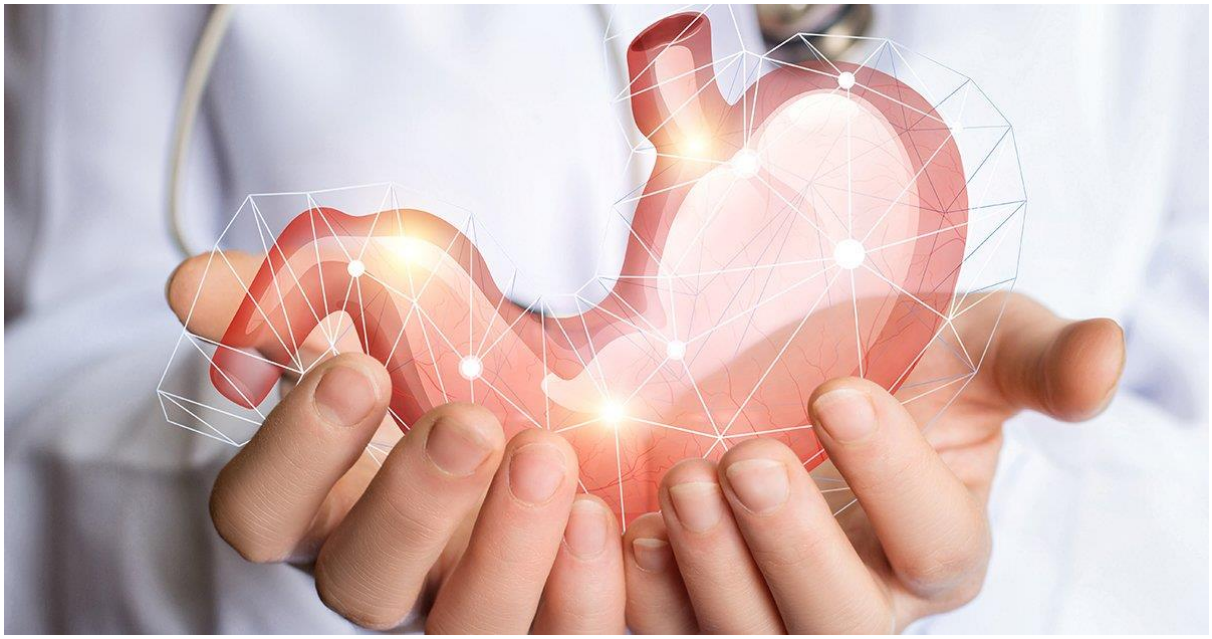
How to cite this article:
Abdul Kader Mohiuddin.Domination of Gastric Complications Among Diabetic Patients.Open Journal of Gastroenterology and Hepatology, 2019, 2:9

eSciPub LLC, Houston, TX USA.
Website: https://escipub.com/

Up to 50% of patients with type 1 and 2 diabetes mellitus (DM) and suboptimal glycemic control have delayed GE, which can be documented with scintigraphy, 13 C-breath tests, or a wireless motility capsule; the remainder have normal or rapid GE [1-3]. Also, it has been determined that 29% of patients with GP had DM [4], 13% developed symptoms after gastric surgery and 36% were idiopathic. About 12% of global health care expenditure ($727 billion) is spent on diabetes. When expanded to the age group between 18 and 99 years, the cost would total to $850 billion. In conjunction with the rising prevalence, the cost is expected to rise to a staggering $958 billion by 2045. In the USA, an estimated 5 million patients suffer from some form of GP, and the female: male ratio is 4:1. Many patients with delayed GE are asymptomatic; others have dyspepsia (i.e., mild-moderate indigestion, with or without a mild delay in GE) or GP, which is a syndrome characterized by moderate-severe upper gastrointestinal symptoms and delayed GE that suggest, but are not accompanied by, gastric outlet obstruction [5]. GP can markedly impair quality of life and up to 50% of patients have significant anxiety and/or depression [1], [6-8]. Woodhouse et.al, 2017 reported combined anxiety/ depression in 24%, severe anxiety in 12%, depression in 23%, and somatization in 50% [6]. In diabetic patients (without neuropathy) and healthy controls, acute hyperglycemia will instead relax the proximal stomach, and suppress gastric electrical activity (e.g., reduced the frequency, propagation, and contraction of the antrum) in both fasting and post-prandial conditions, thereby slowing gastric emptying [9]. Abdominal pain is often epigastric (43%), postprandial (72%), nocturnal (74%), and frequently associated with interference with sleep (66%) [7]. Early satiety (88%), and bloating (64%) were the most common symptoms, however 94% of patients had resolution of their symptoms a year after their operation [10]. Severe/very severe upper abdominal pain occurred in 34% of GP patients and associated with other GP symptoms, somatization, and opiate medication use [11]. Nausea and vomiting are more common in DGP whereas abdominal pain and early satiety are more frequent in idiopathic GP. The 3 main causes of GP are diabetic, postsurgical, and idiopathic [12]. Although GP is frequently associated with diabetes (DGP), idiopathic gastroparesis (IGP) accounts for the majority of cases (60%) [13]. In diabetes, measuring gastric emptying has an additional justification in determining the absorption of orally administered drugs and nutrients, and thus post-prandial glucose regulation. Indeed, new onset or worsening of existing difficulties in blood glucose regulation may be the first symptom of DGP [2]. Growing clinical evidence shows that delayed GE (in GP patients) may be a factor associated with severe reflux, dyspepsia, or both. GP, concomitant in 25% of patients with GERD, has been shown to improve after Nissen fundoplication [14]. Treatment consists of a combination of lifestyle and dietary medication, medications (antiemetics, prokinetics, neuromodulators, and accommodation-enhancers), alternative and complementary therapy, endoscopic therapy (pyloric-directed therapy, temporary stimulation, jejunostomy, or venting gastrostomy) and surgical therapy (pyloroplasty, gastric electrical stimulation, gastrectomy) [15]. In patients with GP, etiologies, symptom severity, and treatments vary among races and ethnicities and between sexes [16]. If a doctor suspects a person with diabetes has GP, he will typically order one or more of the following tests to confirm the diagnosis: Barium X-ray; Barium beefsteak test; Radioisotope gastric-emptying scan; Gastric manometry Blood tests to check for nutritional deficiencies and electrolyte imbalances that are common with GP; Imaging of the gallbladder, kidneys, and pancreas to rule out gallbladder problems, kidney disease, or pancreatitis as causes; An upper endoscopy to check for abnormalities in the structure of the stomach [17]. It is critical to clearly distinguish patients with functional dyspepsia (FD) from

those with GP and to better understand the relationship among alterations in specific symptoms, GE, and altered peripheral and central sensory responses to gastric stimuli [18]. Placebos have been tested in comparison to treatments for GP; however, results general are mixed. For example, Brewer et.al, 2019 reported that RCTs on drug treatments have found placebos can marginally improve overall GP-related symptom scores but placebo effects did not improve gastric emptying [19]. A similar situation may occur in a misguided attempt to improve gastric health by using the ubiquitously prescribed proton pump inhibitors, H2 receptor antagonists, and sucralfate or aluminum hydroxide-based antacids. These drugs are a cause of delayed gastric emptying. Such “therapeutic adventures”, akin to a pyromaniac leading a firefighting operation, may harm rather than improve DGP. A combination of acid-suppressing and prokinetic drugs is indicated only if dyspepsia and GP co-exist with each other [20]. Vagal dysfunction has also been postulated to play a role in DGP. When food is ingested and gastric accommodation is impaired, patients may experience symptoms such as early satiation, fullness and discomfort. Animal and human data suggest that vagal neuropathy can lead to reduction in pyloric relaxation, impaired antral contraction and disturbed antro-pyloric coordination [21]. GP has also been associated with bronchiectasis, aspiration and chronic rejection. GI bleeding secondary to severe refractory esophagitis with an eventual necessity for surgery has also been reported [22]. Most patients respond to conservative treatment with frequent small meals and an upright eating position, in combination with motility agents, such as oral erythromycin analogs, metoclopramide, and domperidone (the last of these is not FDA approved in the US) [23,24]. Metoclopramide and domperidone, a D2 dopamine receptor antagonist, are the most widely used but only metoclopramide is FDA approved in the US while domperidone is available in Europe, Canada, Mexico, and New Zealand [25]. Metoclopramide acts on several different receptors; primarily as a dopamine receptor antagonist, both peripherally improving gastric emptying, and centrally resulting in an anti-emetic effect [26,27]. Metoclopramide side effects, mostly related to its ability to cross the blood-brain barrier, include drowsiness, restlessness, hyperprolactinemia, and tardive dyskinesia (TD) (when taken more than 12 wk), a movement disorder that may be irreversible [28-30]. Other groups of medication, such as 5-HT3 receptor antagonists, phenothiazines, and muscarinic cholinergic receptor antagonist, have been used off-label for symptomatic relieve but they do not have effect of gastric motility. While medications and dietary modification are the first line treatment, approximately 30% of patients do not respond to conservative management. These limitations of medical therapy highlight the need for an alternate therapeutic option [31-35]. Traditional therapy for delayed gastric emptying has focused on supportive treatment, and there is no significant effective therapy. Low-energy shock wave can increase gastric contraction and emptying by activating axonal regeneration and increasing myenteric plexus, but not related with motility peptides [3], [36-38]. Gastric electrical stimulation (GES) (Enterra, Medtronics, Inc.) was approved by FDA in 2000 as a Humanitarian Use Device for patients with refractory diabetic or idiopathic GP [39-41]. On the other hand, high-frequency stimulation (HFS) has no effect on gastric emptying but is able to significantly reduce symptoms of nausea and vomiting in gastroparetic patients. [42,43]. Compared to the use of single point electrodes, the use of two low-resolution electrodes allows recording gastric electrical wave propagation with greater detail. Low resolution recording appears to be superior to single point recordings, while awaiting practical high-resolution recordings [44]. Abell et.al, 2019 concluded that electrical stimulation improves symptoms and physiology with (a) an early and sustained anti-emetic effect; (b) an early and durable gastric

prokinetic effect in delayed emptying patients; (c) an early anti-arrhythmic effect that continues over time; (d) a late autonomic effect; (e) a late hormonal effect; (f) an early anti-inflammatory effect that persists; and (g) an early and sustained improvement in health-related quality of life [45]. GES improved symptoms in 75% of patients with 43% being at least moderately improved. Nausea, loss of appetite, and early satiety responded the best [46,47]. Pain management is essential, as nearly 90% of patients report symptoms of epigastric pain [22]. Pyloric dysfunction has been described in a subset of patients with GP, prompting experimentation with botulinum toxin injections into the pylorus, which is relatively safe and has been successfully used in other gastrointestinal disorders [48]. The measurement of GE using a precise technique such as scintigraphy, which remains as the gold standard, nonetheless provides important mechanistic information when considering the effects on nutrient absorption, postprandial glycemic responses in diabetes, or potential tachyphylaxis [49]. Advances to better understand the pathophysiology and management of DGP have been limited, especially with discordance between symptoms and severity of delay in gastric emptying. Established treatment options are limited; however, recent pharmacologic and surgical interventions show promise [50].



Gastric Complications in Diabetic Patients. Early identification and prompt management of GI complications are of paramount importance as they are associated with significant morbidity. Common GI complications are esophageal dysmotility, gastro-esophageal reflux disease, gastroparesis, enteropathy, NAFLD and glycogenic hepatopathy. Nearly half of patients with DM have delayed GE and some 30% patients having GP was suffering from DM also [1-4].

Acknowledgement

It's a great honor and gratitude to be pharmacists in research and education process. I'm thankful to Dr. Mamun Rashid, Assistant Professor of Pharmaceutics, Appalachian College of Pharmacy Oakwood, Virginia for his precious time to review my article and for his thoughtful suggestions. I'm also grateful to seminar library of Faculty of Pharmacy, University of Dhaka and BANSDOC Library, Bangladesh for providing me books, journal and newsletters.

Abbreviations

Diabetes Mellitus (DM); Gastric Emptying (GE); Gastroparesis (GP); Diabetic Gastroparesis (DGP); Gastroesophageal Reflux Disease

(GERD); Functional Dyspepsia (FD); Gastric Electrical Stimulation (GES); High-Frequency Stimulation (HFS); Randomized Controlled Trials (RCTs); Idiopathic Gastroparesis (IGP); Non-Alcoholic Fatty Liver Disease (NAFLD)

Financial Disclosure or Funding: N/A

Conflict of Interest: The author declares that he has no competing interests.

Informed Consent: N/A

Author contributions: N/A

References

1. Bharucha AE, Kudva YC, Prichard DO. DIABETIC GASTROPARESIS. Endocr Rev. 2019 May 13. doi: 10.1210/er.2018-00161. [Epub ahead of print] PubMed PMID: 31081877.
2. Sangnes DA, Søfteland E, Teigland T, Dimcevski G. Comparing radiopaque markers and (13)C-labelled breath test in diabetic gastroparesis diagnostics. Clin Exp Gastroenterol. 2019 May 7;12:193-201. doi: 10.2147/CEG.S200875. eCollection 2019. PubMed PMID: 31190946; PubMed Central PMCID: PMC6511612.
3. Wu KL, Chiu YC, Yao CC, Tsai CE, Hu ML, Kuo CM, Tai WC, Chuah SK, Hsiao CC. Effect of extracorporeal low-energy shock wave on diabetic gastroparesis in a rat model. J Gastroenterol Hepatol. 2019 Apr;34(4):720-727. doi: 10.1111/jgh.14368. Epub 2018 Jul 29. PubMed PMID: 29966170.
4. Alipour Z, Khatib F, Tabib SM, Javadi H, Jafari E, Aghaghazvini L, Mahmoud-Pashazadeh A, Nabipour I, Assadi M. Assessment of the Prevalence of Diabetic Gastroparesis and Validation of Gastric Emptying Scintigraphy for Diagnosis. Mol Imaging Radionucl Ther. 2017 Feb 5;26(1):17-23. doi: 10.4274/mirt.61587. PubMed PMID: 28291006; PubMed Central PMCID: PMC5350501.
5. Krishnasamy S, Abell TL. Diabetic Gastroparesis: Principles and Current Trends in Management. Diabetes Ther. 2018 Jul;9(Suppl 1):1-42. doi: 10.1007/s13300-018-0454-9. Epub 2018 Jun 22. Review. PubMed PMID: 29934758; PubMed Central PMCID: PMC6028327.
6. Woodhouse S, Hebbard G, Knowles SR. Psychological controversies in gastroparesis: A systematic review. World J Gastroenterol. 2017 Feb 21;23(7):1298-1309. doi: 10.3748/wjg.v23.i7.1298. Review. PubMed PMID: 28275310; PubMed Central PMCID: PMC5323455.
7. Avalos DJ, Sarosiek I, Loganathan P, McCallum RW. Diabetic gastroparesis: current challenges and future prospects. Clin Exp Gastroenterol. 2018 Sep 25;11:347-363. doi: 10.2147/CEG.S131650. eCollection 2018. Review. PubMed PMID: 30310300; PubMed Central PMCID: PMC6165730.
8. Teigland T, Iversen MM, Sangnes DA, Dimcevski G, Søfteland E. A longitudinal study on patients with diabetes and symptoms of gastroparesis - associations with impaired quality of life and increased depressive and anxiety symptoms. J Diabetes Complications. 2018 Jan;32(1):89-94. doi: 10.1016/j.jdiacomp.2017.10.010. Epub 2017 Nov 16. PubMed PMID: 29153755.
9. Aswath GS, Foris LA, Patel K. Diabetic Gastroparesis. [Updated 2019 Apr 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430794/
10. Liu N, Abell T. Gastroparesis Updates on Pathogenesis and Management. Gut Liver. 2017 Sep 15;11(5):579-589. doi: 10.5009/gnl16336. Review. PubMed PMID: 28535580; PubMed Central PMCID: PMC5593319.
11. Parkman HP, Wilson LA, Hasler WL, McCallum RW, Sarosiek I, Koch KL, Abell TL, Schey R, Kuo B, Snape WJ, Nguyen L, Farrugia G, Grover M, Clarke J, Miriel L, Tonascia J, Hamilton F, Pasricha PJ. Abdominal Pain in Patients with Gastroparesis: Associations with Gastroparesis Symptoms, Etiology of Gastroparesis, Gastric Emptying, Somatization, and Quality of Life. Dig Dis Sci. 2019 Mar 9. doi: 10.1007/s10620-019-05522-9. [Epub ahead of print] PubMed PMID: 30852767.
12. Shen S, Xu J, Lamm V, Vachaparambil CT, Chen H, Cai Q. Diabetic Gastroparesis and Nondiabetic Gastroparesis. Gastrointest Endosc Clin N Am. 2019 Jan;29(1):15-25. doi: 10.1016/j.giec.2018.08.002. Epub 2018 Sep 11. Review. PubMed PMID: 30396524.
13. Strijbos D, Keszthelyi D, Smeets FGM, Kruimel J, Gilissen LPL, de Ridder R, Conchillo JM, Masclee AAM. Therapeutic strategies in gastroparesis: Results of stepwise approach with diet and prokinetics, Gastric Rest, and PEG-J: A retrospective analysis. Neurogastroenterol Motil. 2019 Jun;31(6):e13588. doi: 10.1111/nmo.13588. Epub 2019 Apr 4. PubMed PMID: 30947400.
14. Noar MD, Noar E. Gastroparesis associated with gastroesophageal reflux disease and corresponding reflux symptoms may be corrected by radiofrequency ablation of the cardia and esophagogastric junction. Surg Endosc. 2008 Nov;22(11):2440-4. doi: 10.1007/s00464-008-

9873-4. Epub 2008 Apr 24. PubMed PMID: 18437485.

15. Onyimba FU, Clarke JO. Helping Patients with Gastroparesis. Med Clin North Am. 2019 Jan;103(1):71-87. doi: 10.1016/j.mcna.2018.08.013. Review. PubMed PMID: 30466677.
16. Parkman HP, Yamada G, Van Natta ML, Yates K, Hasler WL, Sarosiek I, Grover M, Schey R, Abell TL, Koch KL, Kuo B, Clarke J, Farrugia G, Nguyen L, Snape WJ, Miriel L, Tonascia J, Hamilton F, Pasricha PJ, McCallum RW. Ethnic, Racial, and Sex Differences in Etiology, Symptoms, Treatment, and Symptom Outcomes of Patients With Gastroparesis. Clin Gastroenterol Hepatol. 2019 Jul;17(8):1489-1499.e8. doi: 10.1016/j.cgh.2018.10.050. Epub 2018 Nov 4. PubMed PMID: 30404035; PubMed Central PMCID: PMC6500483.
17. Fletcher J. What to know about diabetic gastroparesis? Reviewed by Saurabh (Seth) Sethi, MD MPH. MedicalNewsToday, April 2019.
18. Kim BJ, Kuo B. Gastroparesis and Functional Dyspepsia: A Blurring Distinction of Pathophysiology and Treatment. J Neurogastroenterol Motil. 2019 Jan 31;25(1):27-35. doi: 10.5056/jnm18162. Review. PubMed PMID: 30509017; PubMed Central PMCID: PMC6326193.
19. Brewer Gutierrez OI, Khashab MA. Stent Placement for the Treatment of Gastroparesis. Gastrointest Endosc Clin N Am. 2019 Jan;29(1):107-115. doi: 10.1016/j.giec.2018.08.011. Review. PubMed PMID: 30396520.
20. Kalra S, Sharma A, Priya G. Diabetic Gastroparesis. Diabetes Ther. 2018 Oct;9(5):1723-1728. doi: 10.1007/s13300-018-0475-4. Epub 2018 Jul 19. PubMed PMID: 30027528; PubMed Central PMCID: PMC6167284.
21. Christophe Vanormelingen, Jan Tack, Christopher N. Andrews, Diabetic gastroparesis, British Medical Bulletin, Volume 105, Issue 1, March 2013, Pages 213–230, https://doi.org/10.1093/bmb/ldt003
22. Navas CM, Patel NK, Lacy BE. Symptomatic Management of Gastroparesis. Gastrointest Endosc Clin N Am. 2019 Jan;29(1):55-70. doi: 10.1016/j.giec.2018.08.005. Epub 2018 Sep 11. Review. PubMed PMID: 30396528.
23. Naik-Mathuria B, Jamous F, Noon GP, Loebe M, Seethamraju H, Bag R. Severe gastroparesis causing splenic rupture: a unique, early complication after heart-lung transplantation. Tex Heart Inst J. 2006;33(4):508-11. PubMed PMID: 17215983; PubMed Central PMCID: PMC1764954.
24. Akindipe OA, Faul JL, Vierra MA, Triadafilopoulos G, Theodore J. The surgical management of severe gastroparesis in heart/lung transplant recipients. Chest. 2000 Mar;117(3):907-10. PubMed PMID: 10713028.
25. Waseem S, Moshiree B, Draganov PV. Gastroparesis: current diagnostic challenges and management considerations. World J Gastroenterol. 2009 Jan 7;15(1):25-37. Review. PubMed PMID: 19115465; PubMed Central PMCID: PMC2653292.
26. Sanger GJ, Andrews PLR. A History of Drug Discovery for Treatment of Nausea and Vomiting and the Implications for Future Research. Front Pharmacol. 2018 Sep 4;9:913. doi: 10.3389/fphar.2018.00913. eCollection 2018. Review. PubMed PMID: 30233361; PubMed Central PMCID: PMC6131675.
27. Abd Ellah NH, Ahmed EA, Abd-Ellatief RB, Ali MF, Zahran AM, Hetta HF. Metoclopramide nanoparticles modulate immune response in a diabetic rat model: association with regulatory T cells and proinflammatory cytokines. Int J Nanomedicine. 2019 Apr 3;14:2383-2395. doi: 10.2147/IJN.S196842. eCollection 2019. PubMed PMID: 31040663; PubMed Central PMCID: PMC6452795.
28. Lee A, Kuo B. Metoclopramide in the treatment of diabetic gastroparesis. Expert Rev Endocrinol Metab. 2010;5(5):653-662. PubMed PMID: 21278804; PubMed Central PMCID: PMC3027056.
29. Shakhatreh M, Jehangir A, Malik Z, Parkman HP. Metoclopramide for the treatment of diabetic gastroparesis. Expert Rev Gastroenterol Hepatol. 2019 Jul 17. doi: 10.1080/17474124.2019.1645594. [Epub ahead of print] PubMed PMID: 31314613.
30. Al-Saffar A, Lennernäs H, Hellström PM. Gastroparesis, metoclopramide, and tardive dyskinesia: Risk revisited. Neurogastroenterol Motil. 2019 May 2:e13617. doi: 10.1111/nmo.13617. [Epub ahead of print] Review. PubMed PMID: 31050085.
31. Mekaroonkamol P, Shah R, Cai Q. Outcomes of per oral endoscopic pyloromyotomy in gastroparesis worldwide. World J Gastroenterol. 2019 Feb 28;25(8):909-922. doi: 10.3748/wjg.v25.i8.909. Review. PubMed PMID: 30833798; PubMed Central PMCID: PMC6397720.
32. Williams PA, Nikitina Y, Kedar A, Lahr CJ, Helling TS, Abell TL. Long-term effects of gastric stimulation on gastric electrical physiology. J

Gastrointest Surg. 2013 Jan;17(1):50-5; discussion p.55-6. doi: 10.1007/s11605-012-2020-5. Epub 2012 Sep 7. PubMed PMID: 22956404; PubMed Central PMCID: PMC5089842.

33. Hasler WL. Newest Drugs for Chronic Unexplained Nausea and Vomiting. Curr Treat Options Gastroenterol. 2016 Dec;14(4):371-385. Review. PubMed PMID: 27726068; PubMed Central PMCID: PMC5814321.
34. Hasler WL. Gastroparesis--current concepts and considerations. Medscape J Med. 2008 Jan 23;10(1):16. Review. PubMed PMID: 18324326; PubMed Central PMCID: PMC2258461.
35. Camilleri M. Pharmacological agents currently in clinical trials for disorders in neurogastroenterology. J Clin Invest. 2013 Oct;123(10):4111-20. doi: 10.1172/JCI70837. Epub 2013 Oct 1. Review. PubMed PMID: 24084743; PubMed Central PMCID: PMC3784550.
36. Atassi H, Abell TL. Gastric Electrical Stimulator for Treatment of Gastroparesis. Gastrointest Endosc Clin N Am. 2019 Jan;29(1):71-83. doi: 10.1016/j.giec.2018.08.013. Review. PubMed PMID: 30396529.
37. Meldgaard T, Olesen SS, Farmer AD, Krogh K, Wendel AA, Brock B, Drewes AM, Brock C. Diabetic Enteropathy: From Molecule to Mechanism-Based Treatment. J Diabetes Res. 2018 Sep 16;2018:3827301. doi: 10.1155/2018/3827301. eCollection 2018. Review. PubMed PMID: 30306092; PubMed Central PMCID: PMC6165592.
38. Demedts I, Masaoka T, Kindt S, De Hertogh G, Geboes K, Farré R, Vanden Berghe P, Tack J. Gastrointestinal motility changes and myenteric plexus alterations in spontaneously diabetic biobreeding rats. J Neurogastroenterol Motil. 2013 Apr;19(2):161-70. doi: 10.5056/jnm.2013.19.2.161. Epub 2013 Apr 16. PubMed PMID: 23667747; PubMed Central PMCID: PMC3644652.
39. Hasanin M, Amin O, Hassan H, Kedar A, Griswold M, Abell TL. Temporary Gastric Stimulation in Patients With Gastroparesis Symptoms: Low-Resolution Mapping Multiple Versus Single Mucosal Lead Electrograms. Gastroenterology Res. 2019 Apr;12(2):60-66. doi: 10.14740/gr1127. Epub 2019 Apr 7. PubMed PMID: 31019614; PubMed Central PMCID: PMC6469903.
40. McCallum RW, Sarosiek I, Parkman HP, Snape W, Brody F, Wo J, Nowak T. Gastric electrical stimulation with Enterra therapy improves symptoms of idiopathic gastroparesis. Neurogastroenterol Motil. 2013 Oct;25(10):815-e636. doi: 10.1111/nmo.12185. Epub 2013 Jul 29. PubMed PMID: 23895180; PubMed Central PMCID: PMC4274014.
41. Lin Z, Forster J, Sarosiek I, McCallum RW. Treatment of gastroparesis with electrical stimulation. Dig Dis Sci. 2003 May;48(5):837-48. Review. PubMed PMID: 12772777.
42. Chu H, Lin Z, Zhong L, McCallum RW, Hou X. Treatment of high-frequency gastric electrical stimulation for gastroparesis. J Gastroenterol Hepatol. 2012 Jun;27(6):1017-26. doi: 10.1111/j.1440-1746.2011.06999.x. Review. PubMed PMID: 22128901.
43. Pasricha TS, Pasricha PJ. Botulinum Toxin Injection for Treatment of Gastroparesis. Gastrointest Endosc Clin N Am. 2019 Jan;29(1):97-106. doi: 10.1016/j.giec.2018.08.007. Epub 2018 Sep 28. Review. PubMed PMID: 30396531; PubMed Central PMCID: PMC6223662.
44. Rayner CK, Jones KL, Horowitz M. Is Making the Stomach Pump Better the Answer to Gastroparesis? Gastroenterology. 2019 May;156(6):1555-1557. doi: 10.1053/j.gastro.2019.03.030. Epub 2019 Mar 26. PubMed PMID: 30926343.
45. Abell TL, Kedar A, Stocker A, Beatty K, McElmurray L, Hughes M, Rashed H, Kennedy W, Wendelschafer-Crabb G, Yang X, Fraig M, Omer E, Miller E, Griswold M, Pinkston C. Gastroparesis syndromes: Response to electrical stimulation. Neurogastroenterol Motil. 2019 Mar;31(3):e13534. doi: 10.1111/nmo.13534. Epub 2019 Jan 31. PubMed PMID: 30706646.
46. Heckert J, Sankineni A, Hughes WB, Harbison S, Parkman H. Gastric Electric Stimulation for Refractory Gastroparesis: A Prospective Analysis of 151 Patients at a Single Center. Dig Dis Sci. 2016 Jan;61(1):168-75. doi: 10.1007/s10620-015-3837-z. Epub 2015 Aug 18. PubMed PMID: 26280084.
47. Parkman HP. Upper GI Disorders: Pathophysiology and Current Therapeutic Approaches. Handb Exp Pharmacol. 2017;239:17-37. doi: 10.1007/164_2016_114. Review. PubMed PMID: 28105529.
48. Parkman HP. Chapter 1. Upper GI Disorders: Pathophysiology and Current Therapeutic Approaches. In: Gastrointestinal Pharmacology Volume 239 of Handbook of Experimental Pharmacology Editor: Beverley Greenwood-Van Meerveld Publisher: Springer, 2017 ISBN 3319563602, 9783319563602
49. Parkman HP. Chapter 24. Gastroparesis, Postprandial Distress. In: Gastrointestinal Motility

Disorders: A Point of Care Clinical Guide Editors: Eytan Bardan, Reza Shaker Publisher: Springer, 2017 ISBN 3319593528, 9783319593524

50. Kumar M, Chapman A, Javed S, Alam U, Malik RA, Azmi S. The Investigation and Treatment of Diabetic Gastroparesis. Clin Ther. 2018 Jun;40(6):850-861. doi: 10.1016/j.clinthera.2018.04.012. Epub 2018 May 7. Review. PubMed PMID: 29748143.