STUDY OF GASTRIC ELECTERICAL CHANGES AND ASSOCIATION WITH HELICOBACTER PYLORI INFECTION IN TYPE 2 DIABETES MELLITUS

Thesis

Submitted for partial fulfillment of Master Degree in Internal Medicine

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قَالُوا سُبْحَانَكَ
لاَ عِلْمَ لَنَا
إِلاَّ مَا عَلَّمْتَنَا
إِنَّكَ أَنتَ
الْعَلِيمُ الْحَكِيمُ
صدق الله العظيم
سورة البقرة الآية (32)

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List of Abbreviations

5-Hydroxytryptamine	**5-HT**
antibody	**Ab**
atrial fibrillation	**AF**
Adenosine tri phosphate	**ATP**
twice daily	**B.d**
bradygastria	**B**
Body mass index	**BMI**
Basement membrane peptidoglycans	**BMPG**
Coronary artery disease	**CAD**
Calibrator factor	**CF**
Chronic gastritis	**CG**
Coronary heart disease	**CAD**
Cycle per minute	**CPM**
Diabetes mellitus	**DM**
Dominant frequency	**DF**
Diabetic gastroparesis	**DGP**
Electrical controlled activity	**ECA**
electrocardiography	**ECG**
Electrogastrography	**EGG**
Expiration:Inspiration ratio	**E:I**
Enzyme linked immunosorbent assay	**ELISA**
Enteric nervous system	**ENS**
Electrical response activity	**ERA**
Fast fourier transform	**FFT**
Fasting plasma glucose	**FPG**
Functional vomiting	**FV**
Glucose-6-phosphatase	**G6P**
Gastric cancer	**GC**
Gastroparesis cardinal symptoms index	**GCSI**
Hydrogen	**H_2**
Glycosylated haemoglobin	**HbA_{1C}**
Homeostasis model assessment insulin resistence	**HOMA-IR**
Helicobacter antigen assay	**HPSA**
Heart rate variation	**HRV**
Irritable bowel syndrome	**IBS**
Interstitial Cell of Cajal with an intramuscular location	**ICC_{IM}**

List of Abbreviations (Cont…)

Interstitial Cells of Cajal in the myenteric region	**ICC_{MY}**
Interlukin	**IL**
Insulin resistence	**IR**
Immune thrombocytopenic purpura	**ITP**
Intra venous	**IV**
Kilogram/ miter^2	**KG/M^2**
Mucosa associated lymphoid tissue lymphoma	**MALT**
Myotonic dystrophy	**MD**
Migratory motor complex	**MMC**
Magnetic resonance image	**MRI**
Normogastria	**N**
N-adenosine di phosphate	**NADP**
Norepinephrine	**NE**
Non steroidal anti inflammatory drugs	**NSAID**
Optical density	**OD**
postprandial plasma glucose	**P.P G**
polymerase chain reaction	**PCR**
Postprandial dip	**PD**
potassium	**K^+**
Proton pump inhibitors	**PPI**
Power ratio	**PR**
Random amplified polymorphic DNA	**RAPD**
Running spectrum analysis	**RSA**
Rapid urease tests	**RUT**
Single photon emission computed tomography	**SPECT**
Three times daily	**t.d.s**
Type 2 Diabetes mellitus	**T2DM**
Type IV secretion system	**T4SS**
Thermo Scientific Pierce	**TSP**
T Helper cells	**TH**
tumour necrosis factor	**TNF**
Urea breath test	**UBT**
Visual analysis	**VA**
Vaculating cytotoxin A	**VacA**
Vasoactive endothelial growth factor	**VEGF**
Vasoactive intestinal peptide	**VIP**

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INTRODUCTION

Diabetes mellitus type 2 – formerly non-insulin-dependent diabetes mellitus (NIDDM) or adult-onset diabetes – is a metabolic disorder that is characterized by high blood glucose in the context of insulin resistence and relative insulin deficiency ***(Kumar et al., 2005).***

Gastroparesis refers to abnormal gastroduodenal motility characterized by delayed gastric emptying in the absence of mechanical obstruction. The etiology is multifactorial and it is now recognized that diabetes is probably the most common cause ***(Chang et al., 2011)***.

The cardinal symptoms include postprandial fullness (early satiety), nausea, vomiting, and bloating. In one tertiary referral series, diabetes accounted for almost one third of cases of gastroparesis. Symptoms attributable to gastroparesis are reported by 5 to 12% of patients with diabetes ***(Camilleri, 2007)***.

Diabetic gastroparesis may cause severe symptoms and result in nutritional compromise, impaired glucose control, and a poor quality of life, independently of other factors such as age, tobacco use, alcohol use, or type of diabetes ***(Camelleri, 2007).***

Electrogastrography (EGG) records gastric myoelectrical activity, known as the slow wave, using cutaneous electrodes affixed to the anterior abdomen overlying the stomach. The slow wave is responsible for controlling the maximal frequency and the controlled aboral propagation of distal gastric contractions ***(Parkman et al., 2004).***

A high prevalence of esophagitis and peptic ulcer was found in *Helicobacter pylori* +ve patients with DM, with or without dyspepsia, especially those with cardiovascular autonomic neuropathy suggesting that this population should be considered as "high risk" for *H.pylori* infection and suitable candidates for treatment. In addition, some data demonstrated a higher prevalence of *H.pylori* infection in diabetic patients with dyspepsia, reactive gastritis and chronic gastritis compared to those with no signs or symptoms of gastrointestinal disease ***(Papamicheal et al., 2009).***

AIM OF THE WORK

Assessment of the gastric electrical changes in type 2 diabetes mellitus patients with upper GIT disturbance and association with Helicobacter pylori infection.

Chapter (1)

GASTRIC MOTOR FUNCTIONS AND GASTRIC ELECTRICAL ACTIVITY

The stomach is the most dilated part of the gastrointestinal tract and has a J-like shape. Positioned between the abdominal esophagus and the small intestine, the stomach is in the epigastric, umbilical, and left hypochondrium regions of the abdomen ***(Drake et al., 2009)***.

- **Gross Anatomy**

The stomach has 4 main regions: the cardia, fundus, body and pylorus. The cardia surrounds the superior opening of the stomach. The rounded portion superior to the left of the cardia is the fundus. Inferior to the fundus is the large central portion of the stomach called the body. The region of the stomach that connects to the duodenum is the pylorus. The pylorus communicates with the duodenum via a smooth muscle sphincter called pyloric sphincter ***(Tortora and Derrickson, 2008).***

- **Microscopic Anatomy**

The innermost lining of the stomach wall is mucosa, which consists of columnar epithelium, lamina propria, and muscularis mucosa. Submucosa contains a rich network of

blood vessels and Meissner's nerve plexus. The smooth muscles of the stomach are arranged in 3 layers: inner oblique (unique to stomach), middle circular (forms the pylorus), and outer longitudinal. Serosa is the visceral peritoneum that covers most of the stomach ***(Eroschenko, 2008).***

- **Blood supply**

Stomach and duodenum drive their blood supply from celiac axis and superior mesenteric artery. The celiac artery branches off as the splenic, left gastric and hepatic arteries. Branches from these vessels including the right gastric and gastroduodenal artery from the hepatic artery and the short gastric arteries and the left gastroepiploic from the splenic artery form an anastomotic network that encircles the stomach ***(Raufman and Goldberg, 2009).***

The inferior pancreaticoduodenal branch of superior mesenteric artery supplies the distal stomach and the duodenum. Corresponding veins course with the arteries and drain into the portal vein ***(Raufman and Goldberg, 2009).***

- **Nerve supply**

The nerve supply includes sympathetic fibers derived from the celiac plexus and parasympathetic fibers from the right and left vagus nerves ***(Snell, 2008).***

The sympathetic innervations of the stomach carry a proportion of pain transmitting nerve fibers where as the parasympathetic vagal fibers are secretomotor to the gastric glands and motor to the motor wall of the stomach. The pyloric sphincter receives motor fibers from the sympathetic system and inhibitory fibers from vagi ***(Snell, 2008).***

Physiology of Gastric Motility

Gastric motility is one of the most critical physiological functions of the human gut. Without coordinated motility, digestion and absorption of dietary nutrients cannot take place. To accomplish its functions effectively, the gut needs to generate not just simple contractions but contractions that are coordinated to produce transit of luminal contents (peristalsis) ***(Yin and Chen, 2010).***

- **Interstitial cells of Cajal and the control of gastric motility**

When electrical recordings are made from the muscle layers of myogenically active regions of the gut, rhythmical waves of depolarization, termed slow waves, are recorded from the smooth muscle cells ***(Hirst and Edwards, 2004).***

Subsequently it was recognized that the muscular wall of the gastrointestinal tract, as well as containing smooth muscle cells, contained a set of specialized cells that lacked contractile elements. These cells are termed Interstitial Cells of Cajal (ICC) and it was suggested, largely from structural studies, that

these cells might be pacemaker cells ***(Hirst and Edwards, 2004).***

In general ICC can be divided into two groups. In most regions of the gastrointestinal tract, a thin layer of ICC forms a network of cells lying between the longitudinal and circular layers in the myenteric region ($ICC_{MY)}$. The second group of ICC has an intramuscular location (ICC_{IM}). The distribution of ICC_{IM} shows regional variation ***(Hirst and Edwards, 2004).***

- **Fasting Gastric Motility**

Fasting gastric contractile patterns are characterized by a cyclic motor phenomenon called the migrating motor complex (MMC). In healthy people, it occurs approximately once every 90 minutes in the fasting state, most prominently at night. The fasting state generally starts approximately 4 hours after meal ingestion, when the stomach has completely emptied a meal ***(Parkman and Jones, 2009)***.

The fasting contractile patterns comprise a period of quiescence (phase I), a period of intermittent pressure activity (phase II), and an activity front during which the stomach and small intestine contract at their highest frequency (phase III). During the phase III migrating motor complex, contraction frequencies reach 3 per minute in the stomach and 11 to 12 per minute in the proximal small intestine ***(Parkman and Jones, 2009)***.