MUCIN SECRETION IN IRRITABLE BOWEL SYNDROME

Thesis Submitted in Partial Fulfilment for
Master Degree in Internal Medicine

By

Sherif Ahmed Nabeeh

SUPERVISORS

Prof. Dr. Mohamed Awad-Alla Sallam
Prof. of Internal Medicine
Ain-Shams University

Dr. Mohsen Maher
Lecturer of Internal Medicine,
Ain-Shams University.

Dr. Salwa Ibrahim El-Haddad
Lecturer of Pathology,
Ain-Shams University.

1987

ERRATA

Page	Line	Mistake	Correction
1	3	is that of long	is IBS that show long
1	13	vlaue	value
1	18	exessively	excessively
4	14	mynetric	myenteric
9	19	prondial	prandial
14	6	Disroders	Disorders
15	12	abdminal	abdominal
25	7	patter	pattern
25	9	condtions	conditions
25	16	distrurbances	disturbances
26	6	tht	that
27	21	enivromental	environmental
31	5	nucosa	mucosa
31	11	Trnasmission	Transmission
32	10	tretment	treatment
33	17	state	stated
33	18	braod	broad
36	7	radition	radiation
37	10	uregency	urgency
37	14	coruse	course
39	14	bluk	bulk
49	5	specially	especially
50	12	accordint	according
50	16	efffect	effect
55	1	atropic	atrophic
56	10	secreling	secreting
63	17	incrased	increased
100	1	inbetween	in between
112	4	center	centers

بسم الله الرحمن الرحيم

2

ACKNOWLEDGEMENT

I would like to express my deepest gratitude to ***Prof. Dr. Mohamed Sallam****, Prof. of Internal Medicine, Ain-Shams University for his fatherly attitude and kind supervision.*

Also, I would like to express my sincere thanks and appreciation for ***Dr. Mohsen Maher****, Lecturer of Internal Medicine, Ain-Shams University for his continuous guidance and providence of all facilities possible to complete this work.*

My deepest thanks also go to ***Dr. Salwa Ibrahim El-Haddad****, Lecturer of Pathology, Ain-Shams University for her professional assistance and great encouragement.*

Last but not least, I wish to express my most profound gratitude to ***Dr. Mahmoud Abdel-Fattah Khalifa****, Lecturer of Pathology, Ain-Shams University who supplied me with the materials used in the different histochemical techniques employed in this work. His valuable guidance and helpful attitude are extremely appreciated.*

w/

CONTENTS

Page

INTRODUCTION

and

AIM OF THE WORK

Introduction

One of the commonest disorders of the alimentary tract is that of long standing dysfunction associated with abdominal pain for which no organic cause can be found. Bowel habit is disturbed by diarrhoea or constipation occuring alone or alternating.

Manometric studies from the distal colon have shown various patterns, when constipation and pain are the pre-dominant symptoms, intra-luminal pressure is usually increased and there is an increased frequency of pressure waves, whereas motor activity is often reduced in patient with painless diarrhoea. These changes are not constant so that motility studies are of no vlaue for diagnostic purposes. Although the aetiology of the irritable bowel syndrome is uncertain up-till-now , the psychological disturbances especially anxiety are frequent. Patients are often tense, conscientious individuals who worry exessively about family or financial affairs (Crean et al, 1985).

The aim of this work is to study the mucin secretion pattern of rectal mucosa in irritable bowel syndrome both qualitatively and quantitatively. Consequently, introduction of an additive criteria for diagnosis becomes at hand.

INTESTINAL MOTILITY

and

ITS DISORDERS

The Physiology of Motility

The intraluminal contents are moved from one specialized region of the gut to another by the coordinated contraction of its smooth muscle layer.
The pattern of motility is integrated with and related to the function of particular regions.

The oesophagus acts as a propulsive conduit for the delivery of food into the stomach which is a mixing and storage organ. Gastric secretion reduces the tonicity of the chyme and this is discharged intermittently into the small intestine where further digestion and absorption take place.

Pattern of motor activity in the small intestine is related to its absorptive function while the colonic movement is related to its role as an organ which conserves water and electrolytes and processes waste material. It is clear that there must be a highly sophisticated control system. Recent years have shown us that it depends on an intrinsic nervous system with multiple neurotransmitters modulated by extrinsic nervous controls (Milla, 1986).

Control of Intestinal Motility

1- Muscle

The power for motility is derived from the smooth muscle coats of the intestine. In the small intestine, they are arranged in three layers: an outer or longitudinal layer which is separated from the inner circular layer by the neural myenteric plexus, the third layer is the muscularis mucosa, the activity of which is poorly understood. The smooth muscle cells are closely attached to one another by tight junctions. This arrangement allows depolarization to spread and take place synchronously through the muscle mass. Intestinal smooth muscle cells have the inherent property of rhythmic variation of transmembrane potential (Milla, 1986).

The cycle of depolarization and repolarization is probably as a result of rhythmic changes in activity of the membrane Na pump (Conner et al , 1974).
Contraction only occurs when an action potential is superimposed on the depolarization plateau.
The regular cycle of depolarization and repolarization or slow wave controls the maximal rate at which contraction may occur. The frequency of the slow wave varies with the region of the gut. In the small intestine, the frequency in the duodenum and upper jejunum is approximately 11 cycles per minute while in the ileum it is slower at about 8 cycles per minute.

2- Nervous control:

The intrinsic and extrinsic innervation is exceedingly complex. The classic view was that of an extrinsic innervation of excitatory cholinergic parasympathetic vagal input and an inhibitory adrenergic sympathetic splanchnic input.

Advances in smooth muscle physiology have revealed a very rich intrinsic innervation, with in addition to traditional cholinergic and adrenergic nerves, non-adrenergic-non-cholinergic (NANC) nerves with many candidate neurotransmitters.
Intestinal cholinergic nerves are predominantly excitatory while adrenergic and NANC nerves are inhibitory.

The mynetric plexus serves as a link between receptor and effector and embodies an intrinsic programme of organized activity. It responds to neural input from both local receptors and higher cortical controls by selecting the appropriate programme (Milla, 1986).

3- Gastrointestinal Polypeptides:

A plethora of peptides capable of affecting intestinal smooth muscle. Theoretically, gastrointestinal peptides might act in three ways: endocrine - as humoral agents

; paracrine - as locally active agents; neurocrine - as neurotransmitters. The latters paracrine and neurocrine modes of action which are of importance in the gut and may act as an additional control system. Five peptides seem to be of importance: Motilin and somatostatin have been implicated in the initiation of phase III activity in the fore and mid gut respectively. Gastrin and cholecystokinin will both distrupt the fasting pattern.

Enkephalins will abolish irregular contractile activity (Milla, 1986).

Patterns of Normal Motility of the Gastrointestinal tract:

Oesophagus

Ingested bollus of food or saliva are propelled from the pharynx to the stomach in some 5-15 seconds by integrated contraction of oesophageal muscle and relaxation of the gastro-oesophageal junction. Peristalsis in the oesophagus differs from that in the intestine as it is not governed by slow wave activity and can be initiated voluntary. Two major elements are clear: a central brain stem regulatory mechanism which controls the coordination of the skeletal muscle involved in sucking and swallowing, together with contraction of the striated muscle of the upper oesophagus and the "off response" of the smooth muscle of the oesophageal body (Milla, 1986).

Stomach:

The stomach functions as a reservoir and as a pump. The fundus and corpus serve as a reservoir and the antrum as a pump. When swallowing occurs, the fundus and corpus resting pressure falls (West, 1984).

Milla (1986), stated that the proximal stomach relaxes in response to swallowing and so accomodates ingested food. This region of the stomach contains the oblique muscle layer and does not exhibit slow wave activity. Innervation is almost entirely derived from inhibitory NANC vagus fibres. The antrum and pylorus are clearly the sites of regulation for the emptying of solids. When a mixed meal is consumed, liquids are emptied more rapidly than solids.

The activity of the stomach changes dramatically when a meal enters the stomach. During the interdigestive period, the stomach passes through cycles of peristaltic waves. The individual waves occur at a rate of 3 cycle per minute and cycle lasts about 5 minute (Hinder ,1983).

The cycle can be broken down into four phases: phase (1) is characterized by the absence of contractions, phase (2) by irregular contractions, phase (3) by a burst of regular large amplitude contractions and phase (4) by a return to quiescence (Code and Marlett, 1975).

The burst of contractions then moves on down the digestive tract to the ileocecal valve, when the cycle ends at the ileocecal valve, a new burst of contractions occurs in the stomach.

Electrophysiological Properties of the Stomach:

The fundic portion of the stomach is electrically silent but the remainder of the stomach shows two types of depolarization: a slow partial depolarization at the rate of 3/minute and a series of rapid greater depolarization superimposed on the others. We refer to the first as slow waves (space setter potentials) and the second as spikes. The first is an inherent property of smooth muscle related to changes in permeability of the cell membrane to sodium, it occurs in the absence of contractions. The second is associated with contractions and represents action potentials. Spikes do not occur in the absence of slow waves and the latter determine the maximal rate of contractions. The slow waves originate in smooth muscle cells located high on the greater curvature of the stomach. These cells constitute the pacemaker. From this site, the slow waves sweep down the stomach to the pylorus. During the interdigestive period, bursts of migrating myoelectric activity begin in the oesophagus and stomach (West, 1984).

Small Intestine:

The function of small intestinal movements is different during the digestive and interdigestive periods. Within the interdigestive phase, the small intestinal motor activity functions to move secretion and shed cells and bacteria into the colon, in cycles of propulsive contractions sweeping from the stomach to the ileocecal valve. After a meal, it is the function of small intestinal motility to mix intestinal content, expose it to a large absorptive surface and gradually move the intestinal stream toward the cecum (West, 1984).

Milla (1986), stated that clear patterns of motility have been described in the small intestine, the patterns of motility present in the fasting state and after food are different. Fasting motility is periodic and feeding abolishes periodicity.

Fasting motor activity:

A periodic pattern of fasting activity was first shown by Szurszewski in 1969. The pattern was characterized