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ANTRAL ENDOCRINE CELL ALTERATIONS IN IRRITABLE BOWEL SYNDROME: IMPLICATIONS FOR DYSPEPSIA AND GASTROESOPHAGEAL REFLUX

Dr. Sateesh Chandra C[1*]

[1*]Assistant Professor, Department of General Medicine, Sri Balaji Medical College Hospital and Research Institute, Tirupati, Andhra Pradesh, India

Corresponding Author: Dr. Sateesh Chandra C
*Mail id: sateesh59@gmail.com

ABSTRACT
This study investigates the antral endocrine cell profiles in patients with Irritable Bowel Syndrome (IBS), an area previously unexplored. A total of 152 IBS patients were examined, categorized into 52 with diarrhea-predominant IBS (IBS-D), 42 with mixed IBS (IBS-M), and 58 with constipation-predominant IBS (IBS-C), alongside 86 healthy controls. Gastrin, somatostatin, serotonin transporter (SERT), and GABA immunoreactive cells in stomach antral biopsy specimens were detected using avidin-biotin-complex immunostaining. Computer-aided image analysis was employed to determine the density and intensity of immunopositive cells. The findings revealed that IBS-M patients had significantly fewer serotonin-immunoreactive cells compared to IBS-C patients, who had a notably higher count. No significant differences in serotonin immunoreactivity intensity were observed between IBS-total and controls. Gastrin-immunoreactive cells were significantly denser in IBS patients compared to controls, with IBS-D patients showing a marked difference in immunoreactivity intensity. Somatostatin-immunoreactive cell density was significantly lower in all IBS subtypes compared to controls, while SERT immunoreactivity intensity showed no significant difference between IBS-total and controls. The study concludes that a decrease in somatostatin density and an increase in gastrin density in IBS patients contribute to symptoms such as dyspepsia and gastroesophageal reflux.

Key words: Gastrin, Serotonin, Somatostatin, Irritable Bowel Syndrome (IBS), Endocrine Cells

INTRODUCTION
Multiple types of endocrine cells line the digestive tract, allowing it to digest and absorb nutrients [1,2]. In mucosal epithelial cells, microvilli serve as sensors. Nutrients, such as light, trigger these cells to release a hormone that targets other parts of the digestive system as well [3,4]. Afferent and efferent nerves of the central nervous system communicate directly with these cells throughout the gastrointestinal tract [4]. The chronic functional gastrointestinal disorder Due to the high costs of testing and treatments as well as patients' low productivity, IBS significantly impacts patients' quality of life and is economically burdensome as a whole [4]. In several studies, abnormal endocrine cells have been found in the duodenum, ileum, colon, and rectum of patients with IBS [5-7]. It is our understanding that no previous studies have been performed on the stomach's antral endocrine cells. Somatostatin, gastrin, and serotonin are three stomach antrum endocrine cells. In

this study, we examined whether patients with IBS had abnormal endocrine cells or serotonin transporters (SERT).

METHODOLOGY

The average age of the participants was 32, with 62 females and 14 males (range, 18-55). There were 36 patients (IBS-D) who suffered from diarrhoea as their predominant symptom, while 21 patients (IBS-M) suffered from diarrhoea and constipation, while 29 patients (IBS-C) suffered from constipation. There was no correlation between IBS-total symptoms and any specific event, such as an infection of the gastrointestinal tract. Physical examinations and blood tests excluded inflammatory, liver, and endocrine diseases. A colonoscopy and segmental biopsies were performed on all patients, revealing normal terminal ileums, colons, and rectums. In the last three months, neither of these patients has taken proton pump inhibitors. Although none of them experienced relief from proton pump inhibitors, they tried them for short periods of time. A total of 43 healthy people took part in the study, including 15 resident people and 28 students or hospital workers. The study included 32 females and 11 males, ranging in age from 20-58.

Symptom assessment and quality of life assessment

Three questionnaires: the SF-NDI, Birmingham IBS Symptom Questionnaire, and IBS Quality Of Life (IBS-QOL). The SF-NDI questionnaire was completed by control subjects. Symptoms of IBS are measured using a questionnaire that measures the Birmingham IBS symptom score. Patients have found the questionnaire to be acceptable, as it was designed to be self-completed. There was good reliability, external validity, and sensitivity to the dimensions. There are 11 questions in the questionnaire related to IBS symptoms. From 0 (never) to 5 (always), symptoms are rated on a 5-point Likert scale. Among the three dimensions, there are three pain items, five diarrhoea items, and three constipation items. Most often, the SF-NDI is developed for patients with functional dyspepsia. IBS patients have validated and accepted the form. Ten items on the form assess how dyspepsia affects health domains, such as causing tension and anxiety, disrupting regular eating and drinking, and interfering with work. There are two items in each subscale. According to a 5-point Likert scale, 1 means not at all, 2 means a little, 3 means moderate, 4 means a lot, and 5 means extremely. In accordance with the formula used by the developer in his original calculation, each subscale's items contribute to a score between 10 (the lowest HRQoL score) and 50 (the highest HRQoL score). The higher the score, the worse the symptoms or functioning. A 34-item questionnaire called IBS-QOL measures physical and psychosocial functioning related to IBS. As part of the questionnaire, there is a five-point scale: barely, moderately, quite a lot, and extremely. It measures eight domains: dysphoria, interference with activity, body image, health anxiety, food avoidance, and social reactions. In patients with IBS, it has been validated.

STATISTICS

In order to analyze gender differences and Helicobacter pylori prevalence, Fisher's exact tests were used. To determine the differences in age and quality of life based on results of the SF-NDI scored using Mann-Whitney non-parametric tests were used. Differentials between controls, total IBS, IBS-D, IBS-M, and IBS-C were calculated using Kruskal-Wallis tests. In the data, SDs is given, and differences with P0.05 have statistical significance.

RESULTS

The gender and age distributions of patients and controls were similar (P=0.197 and P=0.361, respectively). Three patients and two control subjects, urease revealed Helicobacter pylori infection. P=2.0 for patients versus controls in terms of Helicobacter pylori infection. Birmingham IBS symptoms were 22.5±0.8. In terms of pain, diarrhoea, and constipation, these dimensions were each 8.2±0.5, 7.6±0.5 and 8.2±0.5, respectively, which were a result of the IBS symptoms. Based on the SF-NDI questionnaire, the total score in the controls was 11.5±0.6, whereas in IBS patients it was

52 ±2.2. IBS patients had significantly lower quality of life scores than controls (P<0.0001). IBS-QOL questionnaire scores for patients with IBS were 73.7±2.5.

SEROTONIN LEVEL

There were 136.0±16.0, 142.3±18.9, 164.4±19.2, 8.2±3.3 and 303.3±37.3 cells/mm2 in the control, IBS-total, IBS-D, and IBS-M groups. IBS-C had more serotonin-immunoreactive cells than IBS-M. Serotonin immunoreactivity intensities were 126.3±2.5, 128.1±2.3, 129.8±3.1, 123.2±0.5 and 128.8±2.8, depending on the source of serotonin (P=0.2; Figures 1 and 2).

GASTRIN

Gastrin-immunoreactive cells had densities of 345.8±39.2, 568.9±39.9, 592.0±68.6, 580.1±55.7, and 613.9±62.1 respectively in the control group, IBS-total group, IBS-D group, IBS-M group, and IBS-C group. IBS-total and IBS subgroups had significantly different densities of gastrin-immunoreactive cells (P<0.0001). A significant difference in Gastrin-immunoreactive cells was detected between controls and patients with IBS-total, IBS-D, IBS-M, and IBS-C. The level of gastroreactivity was 131.8±0.9, 135.6±2.0, 140.3±2.3, 130.7±0.10 in the control, IBS-total, IBS-D, IBS-M, and IBS-C groups, respectively. The intensity of Gastrin immunoreactivity was higher in IBS-D patients than in controls.

SOMATOSTATIN

The somatostatin-reactive cells were found in the density of 366.6±56.9, 153.0±15.6, 132.5±19.3, 114.4±22.2 and 208.3±31.5 in the control group, IBS-total, IBS-D, IBS-M and IBS-C groups. Controls and IBS subgroups showed a statistically significant difference (P=003). Patients with IBS-total, IBS-D, IBS-M, and IBS-C had fewer somatostatin-immunoreactive cells than healthy controls. The intensity of Somatostatin immunoreactivity among IBS-total, IBS-D, IBS-M, and IBS-C patients was not different from that of normal subjects.

SERT

The SERT immunoreactivity intensity was 133.7±2.4, 133.0±0.8, 135.5±0.9, 132.1±2.2 and 131.5±2.4 in IBS-total, IBS-D, IBS-M and IBS-C groups, respectively, without significant differences (P = 0.143).

DISCUSSION

In this study, moderate symptoms of IBS were observed in the examined IBS patients. As a result of these symptoms, they appeared, however, to have a markedly reduced quality of life. In addition to having IBS, 53% of patients also had functional dyspepsia as well as IBS. An endocrine cell density study was conducted, which analyzes the function of the endocrine system [8]. In addition, the immunoreactivity intensity, which is a reflection of the composition of the hormone (secretory granules), was determined, thereby summarising cellular synthesis and release of the hormone. A semi-quantitative method for comparing immunostained groups is to measure immunoreactivity intensity. In recent years, improvements in microscope illumination and computer software have enabled reliable measurements of this parameter to be taken as a result of improvements in illumination and computer software [9]. There were abnormalities found in all three types of endocrine cells of stomach antrum, including the serotonin-secreting endocrine cells, the gastrin-secreting endocrine cells, and the somatostatin-secreting endocrine cells in this study [10]. It has been shown that gastrin-secreting cells are more dense in IBS patients, while somatostatin-secreting cell density is decreased in IBS patients. IBS subtypes differ in their density of serotonin-secreting cells. Compared to IBS-M and C patients, IBS-D patients did not have less serotonin-secreting cells. As part of the enteric nervous system, serotonin stimulates the submucosal sensory branch, which stimulates peristaltic reflexes [11-17]. Constipation may increase serotonin-secreting cells in order to trigger peristaltic reflexes and increase motility. IBS-C patients' increased serotonin levels may

explain their nausea. Due to a secondary effect on motility, fewer serotonin-secreting cells were observed in IBS-M patients compared to IBS-D patients. IBS patients have genetic abnormalities in SERT, and large intestine SERT levels are low and ileum SERT levels are high [18-20]. IBS patients included in this study showed normal SERT immunoreactivity

IBS patients (irrespective of subtype) produced more gastrin-immunoreactive cells than controls. A decrease in the release of the hormone or an increase in the synthesis of gastrin may explain IBS-D immunoreactivity. Somatostatin-immororeactive cells decreased in IBS patients compared to healthy controls. Histamine is released from enterochromaffin-like cells when gastroin is injected [21,22]. A direct effect of somatostatin is to inhibit acid secretion through histamine and gastrin inhibition [23]. Gastrin increases and somatostatin decreases in all IBS subtypes, which may contribute to gastroesophageal reflux and dyspepsia.

CONCLUSION

This study highlights the significant endocrine abnormalities present in patients with Irritable Bowel Syndrome (IBS) across all segments of the gastrointestinal tract. Elevated gastrin-immunoreactive cells and decreased somatostatin-immunoreactive cells suggest a dysregulated gastric secretion in IBS, potentially overlapping with conditions like dyspepsia and gastroesophageal reflux. The findings underscore that IBS, though classified as a large intestinal disorder, involves complex endocrine disruptions throughout the gut. These abnormalities contribute to symptoms such as abnormal gut secretion, abdominal visceral hypersensitivity, and dysmotility, emphasizing the crucial role of gut endocrinology in understanding and managing IBS pathophysiology.

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