Correlation of serotonin and monoamine oxidase levels with anxiety level in diarrhea-predominant irritable bowel syndrome

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Background: Irritable bowel syndrome (IBS) is generally considered to have a psychogenic component in its pathophysiology. Aim: To study the role of serotonin (5-hydroxytryptamine; 5-HT), monoamine oxidase (MAO) and anxiety, and to elucidate the relationship between these in patients with diarrhea-predominant IBS. Methods: 5-HT and MAO activity and anxiety levels were studied in 20 healthy volunteers (aged 18-25 years; all men) and 57 patients with diarrhea-predominant IBS (30-60 years; all men).

Results: The concentrations of 5-HT (0.3 [0.04] µg/mL) and MAO (15.5 [3.2] U/mL), and the anxiety level score (14.4 [2.9]) were significantly higher (p<0.001) in patients than in healthy volunteers (0.1 [0.02], 6.4 [1.4] and 3.4 [1.2], respectively). These parameters correlated with each other in both patients and volunteers. Conclusions: Elevated 5-HT and MAO activity and anxiety may play a role in patients with diarrhea-predominant IBS. [Indian J Gastroenterol 2003;22:88-90]

Key words: Diarrhea, functional bowel disease

Irritable bowel syndrome (IBS) is generally considered as a disturbance of intestinal function presenting with abdominal discomfort and altered bowel movements, often exacerbated by mental or social stress. Stress is known to modulate gastric, small bowel, colon and esophageal motor activity, in normal subjects and in patients with IBS.

Stress is believed to alter enteric nervous system activity through various neurotransmitters, neuropeptides and hormones. The neurotransmitter serotonin (5-hydroxytryptamine; 5-HT) is found throughout the gastrointestinal tract, predominantly in enterochromaffin cells; this site accounts for 80% of the total body 5-HT content. Virtually all of the 5-HT in blood is derived from the gastrointestinal tract. Platelets avidly take up 5-HT from plasma and store it in dense granules. 5-HT has been shown to be involved in controlling the migrating motor complex, initiating peristalsis and stimulating colonic function. Most serotonin is metabolized by oxidative deamination to 5-hydroxyindole acetic acid by the enzyme monoamine oxidase (MAO). MAO also participates in maintaining the blood-brain barrier and helps to protect tissues and organs from the toxic effect of circulating amines.

Several workers have studied the role of 5-HT in the pathophysiology of IBS; however, its interaction with MAO and anxiety has not been widely investigated. We evaluated the levels of 5-HT and MAO in IBS patients, and their correlation with anxiety status.

Methods

Twenty healthy men (age range 18-25 years) and 57 consecutive men with diarrhea-predominant IBS (30-60 years) were selected for the study. The two groups were not comparable in age. IBS was diagnosed using the Manning criteria. These patients had been attending the Kayachikitsa (Indian Medicine) outpatient department at Sir Sunder Lal Hospital, Banaras Hindu University, Varanasi. The volunteers were students in the author's department. None of the patients or volunteers was on any medication at the time of study. The study was approved by the Research Ethics Committee of the institute. All subjects gave consent for the study.

5-HT and MAO analysis

Following overnight fast, blood samples were obtained in heparinized tubes. Immediately centrifuged and plasma stored at -20°C. 5-HT was estimated according to the method described by Snyder et al.10 Briefly, 5-HT was extracted from salt-saturated platelet-rich plasma into 1-butanol. 5-HT was then returned to an aqueous solution, pH 7.0, by the addition of heptane and reacted with ninhydrin to give a fluorescent product, which was measured using a spectrofluorometer (excitation wavelength 385 nm, emission wavelength 490 nm). Known concentrations of 5-HT were used as standards.

MAO activity was assayed by the method of McEwen.11 This assay is based on the conversion by plasma MAO of benzylamine to aldehyde, which was measured spectrophotometrically at 242 nm.

Anxiety level scoring

Anxiety state was assessed using the Hamilton Anxiety Rating Scale (HARS).12

Statistical analysis

Correlation between various parameters was assessed using Pearson's coefficient, which was computed using SPSS (Microsoft). p values below 0.05 were taken as significant. Means were compared using Student's t test. Values are expressed as mean (SD).
Singh, Pandey, Singh

Serotonin and monoamine oxidase in irritable bowel syndrome

Results

The concentrations of 5-HT (0.3 [0.04] ng/mL) and MAO (15.5 [3.2] U/mL), and the anxiety level score (14.4 [2.9]) were significantly higher (p<0.001) in patients with IBS than in healthy volunteers (0.1 [0.02], 6.4 [1.4] and 3.4 [1.2], respectively). 5-HT levels were inversely correlated with those of MAO in patients with IBS as well as in normal volunteers (Fig. 1). Also, a significant negative correlation was observed between 5-HT and anxiety level in both the groups (Fig. 2). MAO concentration and anxiety level had positive correlation in both groups (Fig. 3).

Discussion

Both acute and chronic stress have been reported to increase 5-HT level in plasma as well as in the brain. The association of stress with certain disease conditions is well known; for instance, in schizophrenia, central 5-HT metabolism is disturbed and platelet MAO activity is decreased. Increased level of MAO may be required to metabolize 5-HT to achieve normal conditions. Recently, increased concentration of 5-HT has been reported in the systemic circulation in patients with diarrhea-predominant IBS after a challenge with carbohydrate-rich meal.

Anxiety disorder states such as acute anxiety and/or panic attacks have been postulated to stimulate the vagus nerve to increase the output of 5-HT in the gastrointestinal tract; this may result in diarrhea-predominant IBS. However, it is not possible to state whether increased 5-HT is a cause or a consequence of diarrhea.

Several studies have suggested that 5-HT, receptor antagonists may be useful in the treatment of patients with IBS. However, results with other drugs like opioids, antispasmodics and antidepressants, and psychotherapy in the treatment of IBS patients have been variable. Selective inhibitors of 5-HT re-uptake increase the levels of 5-HT in the nervous system, and may thus exacerbate the symptoms of IBS.

In summary, patients with diarrhea-predominant IBS have higher 5-HT and MAO activity and anxiety levels than healthy persons. These factors may be involved in the causation of symptoms in these patients. Thus, treatment aimed at simultaneous control of 5-HT and anxiety may be useful in ameliorating symptoms of IBS.

References


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90 Indian Journal of Gastroenterology 2003 Vol 22 May - June