

Sex Specific Alterations In Autonomic Function In Patients With Irritable Bowel Syndrome.

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Abstract:

Background: Autonomic nerve function impairment is related to development of Irritable Bowel Syndrome (IBS). Heart rate variability (HRV) is a useful tool to measure autonomic nerve function activity and also sympatho-vagal balance.

Objective: To assess autonomic nerve function activity by heart rate variability analysis in male and female patients with Irritable Bowel Syndrome.

Methods: This cross sectional study was conducted in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from 1st July 2010 to 30th June 2011. Ninety patients aged 20-50 years of both sexes with Irritable bowel syndrome were included in the study group. They were collected from the OPD of Gastroenterology in BSMMU. For comparison age and sex matched 30 apparently healthy subjects were also studied as control. The power spectral HRV parameters were recorded by a digital Polyrite. For statistical analysis independent sample t-test was performed as applicable.

Results: Mean resting pulse rate, mean HR, SBP, DBP, LF, LF norm and LF/HF were significantly higher and total power, HF, HF norm were significantly lower in female IBS group than male IBS group when compared to those of control.

Conclusion: This study concludes markedly lower parasympathetic with concomitant higher sympathetic activity and shifting of sympathovagal balance towards sympathetic predominance in female than that of male IBS patients.

Key words: Irritable bowel syndrome, Autonomic nerve function, Heart rate variability

Introduction :

Irritable bowel syndrome is a chronic continuous or remittent functional gastrointestinal disorder, characterized by abdominal pain, bloating and bowel disturbance.¹ This disease holds a major share in gastrointestinal tract related health problem. The prevalence rate of this disease was 24.4% in rural community and 7.7% in urban community of Bangladesh and the male female ratio of this disorder was 1:1.36.²

Three subgroups of IBS patients were defined on the basis of Rome supportive symptoms. It includes diarrhea predominant IBS (IBS-D), constipation predominant IBS (IBS-C), and IBS with alternate bowel habit (IBS-A).²

On the basis of abdominal and bowel symptoms IBS was diagnosed and classified by revised Rome-II criteria.³ The criteria for diagnosis of IBS include abdominal discomfort or pain where at least two of the features are to be present which is relieved by

defecation, onset is associated with a change in frequency and form of stool. The symptom must persist at least 12 weeks, in the preceding one year.²

According to literature, IBS is multifactorial in origin. Several environmental factors, psycho social stressors, altered gut flora contribute to pathophysiology of IBS. It is now largely considered as a disorder of the brain-gut axis, involving abnormal function in the enteric, autonomic and central nervous system.⁴

Autonomic nervous system regulates the visceral sensitivity of the body and coordinates gastrointestinal motility and secretion.⁵ Recent studies reported that autonomic nervous system may be affected by inflammatory reaction at the level of enteric mucosa.⁶

Heart rate variability (HRV) is a measure which reflects autonomic nervous control. Normally HR variation is related to the balance between sympathetic & parasympathetic nervous system which provides early better qualitative and quantitative interpretation of sympathovagal modulation and can detect autonomic impairment.¹⁰

Higher HRV indicates good adaptability and well functioning autonomic control. On the other hand, reduced heart rate variability acts as a strong predictor of risk for adverse events with wide range of diseases.⁷

Among the power spectral measures the total power indicates the total variability of cardiac autonomic nervous activity brought about by continuous vagal modulation. LF power, LF norm represents sympathetic activity whereas HF power, HF norm represents parasympathetic activity. In addition LF/HF represents the sympatho-vagal balance of autonomic control.

Various investigators of different countries reported lower values of LF, HF, LF/HF and LF norm in patients with IBS compared with those of healthy control.^{8,9} On the contrary some researchers found higher values of these parameters in IBS patients.^{8,10,11-13}

In Bangladesh, 7.7% prevalence rate of IBS is reported. The high incidence of IBS in our country deserves greater attention. It has been suggested that IBS patients suffer from physical ailments as well as mental anxiety and depression which in turn may be related to their disordered autonomic nerve function. Many studies in other countries investigated on autonomic nerve function in this group of patients and they explored the contribution of autonomic nerve dysfunction to many of the symptoms of IBS. But the results of these

investigations are conflicting or uncertain. In our country, several studies on autonomic nerve functions was done by microcomputer based time and frequency domain methods on hyperthyroidism¹⁴, athletes¹⁵, sedentary workers¹⁶, essential hypertension¹⁷ and rheumatoid arthritis¹⁸. But, yet no published data was available to document the changes of HRV in Irritable bowel syndrome by HRV spectral analysis.

Therefore, this study was carried out to assess the autonomic nerve function status in IBS patients in order to confirm its role in occurrence of this disease. This study also aimed to evaluate the importance of autonomic nerve function test as screening test in IBS patient for detecting autonomic neuropathy. Furthermore this study also attempted to find out any difference in autonomic nerve function in different subtypes of IBS.

Methods:

This cross sectional study was conducted in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka from July 2010 to June 2011. Study subjects were selected by following simple random sampling procedure and the protocol of this study was approved by central ethical review committee of BSMMU. Total 90 patients of Irritable Bowel Syndrome (IBS), 45 male and 45 female aged 20-50 years were enrolled in the study group (Group B). According to Rome supportive symptoms criteria based on bowel habit predominance, patients of IBS were subdivided to, B₁ consists of 30 patients showing symptoms of diarrhea predominance IBS (IBS-D), B₂ consists of 30 patients showing symptoms of constipation predominance IBS (IBS-C) and B₃ consists of 30 patients with alternating bowel habits IBS (IBS-A) showing symptoms of both diarrhea predominance IBS (IBS-D) and constipation predominance IBS (IBS-C). Data in all IBS groups were compared with age and sex matched 30 apparently healthy subjects (Group A) as well as among the disease subgroup. The patients were collected from out patient Department of Gastroenterology, (BSMMU), Dhaka and the healthy subjects of control group was selected by personal contact. IBS patients with history of heart diseases, hypertension, diabetes mellitus, chronic renal failure, habit of smoking, pregnancy and thyroid disorder were excluded from the study. Autonomic nerve function test of all subjects were done by power spectral analysis of HRV.

After selection, the subject was thoroughly informed about the risk and benefit and detail procedure of the study before examination and collection of blood sample. For recording of the HRV parameters subjects were prepared from the previous day of examination. An informed written consent was taken. They were advised to finish their meal by 9:00 pm on the previous night, to remain free from any physical or mental stress, not to take sedatives or any drugs affecting nervous system and to have a sound sleep at night. The subjects were also asked to have light breakfast without tea or coffee. All examinations were done in the Autonomic Nerve Function Test Laboratory in the Department of Physiology of Bangabandhu Sheikh Mujib Medical University between 9a.m. to 1 p.m. Detail history was taken and thorough physical examinations were done. All informations were recorded in a prefixed data schedule. For Autonomic Nerve Function Test the subject lied on a bed in supine position and allowed to take rest for 15-20 minutes. 5 minutes ECG recording for HRV was taken by a polygraph. Power spectral measures of HRV data were expressed in mean and SD. For statistical analysis unpaired t- test was done.

Results :

All the groups were matched for age and BMI. Mean values of resting pulse rate, SBP and DBP were significantly higher in group B1_F, B2_F and B3_F than that of group A_F and non significantly higher in group B1_M, B2_M and B3_M than that of group A_M. (Table I) The mean total power, HF and HF norm were significantly lower and LF, LF norm and LF/HF were significantly higher in group B1_F, B2_F and B3_F than that of group A_F and again the mean total power, HF and HF norm were non significantly lower and LF, LF norm and LF/HF were non significantly higher in group B1_M, B2_M and B3_M than that of group A_M. (Table II & III)

Table I: Resting Pulse rate and BP in different groups (n=120)

Groups	Pulse (beat/min)	SBP (mm of Hg)	DBP (mm of Hg)
A _M (n=15)	73±7.35	112±5.32	72±5.68
A _F (n=15)	76±8.65	114±6.89	69±9.47
B1 _M (n=15)	76±3.25	15±6.54	74±5.32
B1 _F (n=15)	90±6.58	29±9.54	76±8.24
B2 _M (n=15)	75±5.21	114±2.51	76±5.24
B2 _F (n=15)	89±2.14	127±4.26	79±5.54
B3 _M (n=15)	76±3.58	116±5.85	75±9.57
B3 _F (n=15)	91±2.25	28±10.52	80±8.96

Statistical analysis

Groups	p value		
A _M vs.B1 _M	0.455 ^{ns}	0.957 ^{ns}	0.473 ^{ns}
A _M vs.B2 _M	0.487 ^{ns}	0.578 ^{ns}	0.851 ^{ns}
A _M vs.B3 _M	0.140 ^{ns}	0.595 ^{ns}	0.529 ^{ns}
A _F vs.B1 _F	0.000 ^{***}	0.002 ^{**}	0.032 [*]
A _F vs.B2 _F	0.000 ^{***}	0.003 ^{**}	0.007 ^{**}
A _F vs.B3 _F	0.000 ^{***}	0.018 [*]	0.003 ^{**}

Data were expressed as Mean ± SD. Data analysis was done by Independent sample t-test.

SBP= Systolic blood pressure, DBP=Diastolic blood pressure

*** = p<0.001 , ** = p<0.01, * = p<0.05 , ns = non significant (p>0.05)

n = number of subjects. M=male. F=female.

Group A: Apparently healthy subjects (control)

Group B1: Diarrhea predominant Irritable Bowel Syndrome (IBS-D)

Group B2: Constipation predominant Irritable Bowel Syndrome (IBS-C)

Group B3: Irritable Bowel Syndrome with alternate bowel habit (IBS-A)

Table II: Power Spectral measures of HRV in different groups (n=120)

Groups	Total power (ms ²)	LF (ms ²)	HF (ms ²)
A _M (n=15)	1878.4±287.3	795.3±69.3	510.2±53.4
A _F (n=15)	1950.4±249.2	820.9±52.5	525.2±54.3
B1 _M (n=15)	1780.3±258.9	816.9±184.0	453.5±77.1
B1 _F (n=15)	1646.2±338.4	902.2±125.3	356.2±32.9
B2 _M (n=15)	1796.5±365.5	805.6±196.4	461.5±98.7
B2 _F (n=15)	1671.1±330.5	935.5±125.3	325.1±63.4
B3 _M (n=15)	1805.3±235.9	809.2±206.8	456.6±85.1
B3 _F (n=15)	1675.3±315.5	920.2±142.3	341.1±63.2

Statistical analysis

Groups	p value		
A _M vs.B1 _M	0.953 ^{ns}	0.659 ^{ns}	0.728 ^{ns}
A _M vs.B2 _M	0.431 ^{ns}	0.940 ^{ns}	0.839 ^{ns}
A _M vs.B3 _M	0.402 ^{ns}	0.726 ^{ns}	0.882 ^{ns}
A _F vs.B1 _F	0.000 ^{***}	0.000 ^{***}	0.000 ^{***}
A _F vs.B2 _F	0.000 ^{***}	0.001 ^{**}	0.000 ^{***}
A _F vs.B3 _F	0.000 ^{***}	0.001 ^{**}	0.000 ^{***}

Data were expressed as Mean \pm SD. Data analysis was done by Independent sample t-test.

LF= Low frequency, HF= High frequency, ms²= squared millisecond.

*** = p<0.001, ** = p<0.01, ns = non significant (p>0.05).

n = number of subjects. M=male. F=female.

Group A: Apparently healthy subjects (control)

Group B1: Diarrhea predominant Irritable Bowel Syndrome (IBS-D)

Group B2: Constipation predominant Irritable Bowel Syndrome (IBS-C)

Group B3: Irritable Bowel Syndrome with alternate bowel habit (IBS-A)

Table III: Power Spectral measures of HRV in different groups (n=120)

Groups	LF norm (n.u)	HF norm (n.u)	LF/HF
A _M (n=15)	54.17 \pm 5.50	35.14 \pm 6.21	1.54 \pm 0.26
A _F (n=15)	59.47 \pm 5.36	39.25 \pm 5.64	1.51 \pm 0.68
B1 _M (n=15)	63.12 \pm 7.26	29.30 \pm 4.04	2.35 \pm 1.03
B1 _F (n=15)	73.25 \pm 5.36	24.61 \pm 3.25	3.15 \pm 2.56
B2 _M (n=15)	59.19 \pm 7.28	32.31 \pm 6.84	2.12 \pm 1.12
B2 _F (n=15)	79.19 \pm 6.21	21.51 \pm 5.69	3.20 \pm 3.68
B3 _M (n=15)	62.25 \pm 5.58	30.05 \pm 4.02	2.14 \pm 0.84
B3 _F (n=15)	82.25 \pm 2.56	26.28 \pm 9.58	3.54 \pm 1.24

Statistical analysis

Groups	p value		
A _M vs. B1 _M	0.625 ^{ns}	0.176 ^{ns}	0.487 ^{ns}
A _M vs. B2 _M	0.074 ^{ns}	0.570 ^{ns}	0.469 ^{ns}
A _M vs. B3 _M	0.208 ^{ns}	0.235 ^{ns}	0.974 ^{ns}
A _F vs. B1 _F	0.000 ^{***}	0.000 ^{***}	0.000 ^{***}
A _F vs. B2 _F	0.000 ^{***}	0.000 ^{***}	0.000 ^{***}
A _F vs. B3 _F	0.000 ^{***}	0.000 ^{***}	0.000 ^{***}

Data were expressed as Mean \pm SD. Data analysis was done by Independent sample t-test.

LF (nu) = Low frequency in normalized unit, HF (nu) = High frequency in normalized unit.

LF/HF = Ratio of low frequency and high frequency.

*** = p<0.001, ns = non significant (p>0.05).

n = number of subjects. M=male. F=female.

Group A: Apparently healthy subjects (control)

Group B1: Diarrhea predominant Irritable Bowel Syndrome (IBS-D)

Group B2: Constipation predominant Irritable Bowel Syndrome (IBS-C)

Group B3: Irritable Bowel Syndrome with alternate bowel habit (IBS-A)

Discussion :

In the recent study, values of HRV parameters in healthy subjects were almost within normal range and also similar to those reported by the various investigators from different countries^{9-11, 19} as well as from our country.¹⁴⁻¹⁸

In this study, significantly higher values of mean resting pulse rate, mean heart rate, systolic blood pressure, diastolic blood pressure, LF power, LF norm and LF/HF represents higher sympathetic activity in female IBS patients irrespective of subgroups. Similar types of findings were also reported by the various investigators of different countries.^{9-10, 13, 19, 20} But the results could not show any significant difference in sympathetic activity among the subtypes of IBS patients.

The total power, HF power, HF norm were significantly lower in female IBS patients which indicate lower parasympathetic activity. Similar findings were also observed by the various investigators of different countries.^{8,9,10,13} But the results could not discriminate parasympathetic activity among the subtypes of IBS patients. Lack of differences among the subtypes of IBS patients may be due to predominance of autonomic enteric nervous system activity.³

Different investigators explained various mechanisms for involvement of autonomic nerve function activity in IBS patients. Increased release of corticotrophin releasing factor (CRF) from hypothalamus affect directly or through locus ceruleus. It stimulate anxiety, bowel motility and sympathetic tone.⁹

Anxiety, depressive disorder and emotional state cause lower parasympathetic nervous system activity. This may alter autonomic nervous system input to the gastrointestinal system.¹⁹ It has also been suggested that this autonomic nerve dysfunction may influence the descending inhibitory pathway and increase bowel sensitivity.

In the present study, HRV analysis showed increased sympathetic activity and reduced vagal tone. Again, significant changes of all the HRV parameters indicate shifting of sympathovagal balance towards sympathetic predominance. These features represent autonomic dysfunction in the present series of patients. This dysfunction is most likely attributed to anxiety, depressive disorder, somatization disorder, psychological distress, emotional state. This view may not be confirmed as anxiety, depressive disorder, somatization disorder, psychological distress, emotional states were not investigated in this study.

Conclusions :

In the present study, autonomic nerve function activity in male and female IBS patients was studied by analysis of HRV parameters. Markedly decreased parasympathetic with increased sympathetic activities was found by this analysis in female patients of present series. All these changes indicate impaired autonomic nerve function in female patients with irritable bowel syndrome.

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