EVALUATION OF AUTONOMIC NERVE FUNCTIONS BY TESTING CARDIOVASCULAR REFLEXES IN IRRITABLE BOWEL SYNDROME

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Abstracts: **Background:** Irritable bowel syndrome (IBS) is a common disease and its etiology is still uncertain and not much information available concerning cardiovascular reflexes signifying changes in autonomic nerve functions in IBS. The aim of the present study therefore was to study autonomic nerve functions by testing cardiovascular reflexes in patients of IBS. An attempt was made to assess the response in various clinical varieties of IBS and to study if any autonomic change present has some correlation with duration of IBS. **Material and method**: This study was carried out on 30 patients of Irritable bowel syndrome and 30 healthy individuals as a control group. Diagnosis of Irritable Bowel Syndrome was made by exclusion criteria and Rome IV criteria. The five tests were performed to assess the cardiovascular responses to autonomic nerve functions in patients of Irritable Bowel Syndrome and control group. **Results**: Symptoms of autonomic irritability noted in IBS patients which may be due to anxiety and tension states and that aspect is to be evaluated separately. Results of five cardiovascular reflexes performed in patients of IBS were statistically insignificant (P>0.1). **Conclusion**: No evidence of autonomic neuropathy in IBS patients was seen neither any impairment of the cardiovascular response to various autonomic tests was present with increasing duration of disease or with advancing age in irritable bowel syndrome patients.

Key Words: Irritable Bowel Syndrome (IBS), cardiovascular reflexes, autonomic.

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Introduction: IBS is a recurring, chronic gastrointestinal disorder that's characterised by:
Unexplained abdominal discomfort and pain.
Changes in bowel habit (i.e., constipation, diarrhoea, or a mix of constipation and diarrhoea) and consistency.
An IBS diagnosis is largely based on symptoms due to the lack of positive pathological tests.
Gastroenterologists use the Rome IV criteria to diagnose IBS, the Rome IV criteria are as follows:
Recurrent abdominal pain, on average, at least one day per week in the last 3 months, associated with two or more of the following criteria:
Related to defecation.
Associated with a change in frequency of stool.
Associated with a change in form (appearance) of stool.
This affect the person's quality of life, both professionally and socially [1, 2].
The world-wide prevalence of IBS is 11.2% (95% confidence interval: 9.8%-12.8%) based on a meta-analysis of 80 studies involving 260,960 subjects [3].
In the United States, as many as 15% of adults report IBS symptoms [4]. The prevalence of IBS varies from 4.2%-7.5%, 7.7%-12.9% and 11%-14% in India, Bangladesh and Malaysia, respectively [5]. 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 [6]. Autonomic nervous system regulates the visceral sensitivity of the body and coordinates gastrointestinal motility and secretion [7]. Recent studies reported that autonomic nervous system may be affected by inflammatory reaction at the level of enteric mucosa [8]. Very few studies are available in literature concerning cardiovascular reflexes signifying changes in autonomic nerve functions in IBS. Therefore, it appears worthwhile to evaluate autonomic nerve functions (by testing cardiovascular reflexes) in patients of IBS least they should have a role in the aetiology of the disease.

The autonomic nerve function tests used in the present project to study the cardiovascular responses in patients of IBS are: Heart rate response to Valsalva manoeuvre, Immediate heart rate response to standing, Beat to beat variation of heart rate to single deep breath, Isometric hand-grip test, Blood pressure response to standing.

The aim of the present study therefore was to study autonomic nerve functions by testing cardiovascular reflexes in patients of IBS. An attempt was made to assess the response in various clinical varieties of IBS and to study if any autonomic change present has some correlation with duration of IBS.

Material and Methods: This study was carried out on 30 patients of Irritable bowel syndrome admitted in medical ward and OPD in Mamata Medical College and 30 healthy individuals, closely matched for age and sex served as a control group. A detailed clinical history and clinical examination was recorded for each patient. Patients of cardio-respiratory disease, amyloidosis, porphyria, chronic renal failure, chronic alcoholism, collagen diseases, tuberculosis, malignancy of any site, hypertension, thyrotoxicosis, diabetes mellitus and on drug therapy especially β blockers and parasympatholytics were excluded from the study.

The patients of Irritable Bowel Syndrome were divided into three groups.

(a) Patients with spastic colon variant
(b) Patients with painless diarrhea.
(c) Patients with alternating diarrhea and constipation.

Diagnosis of Irritable Bowel Syndrome was made by exclusion criteria and Rome IV criteria [1, 2].

X-ray chest was taken in all patients to exclude any pathology in the chest. Full 12 leads ECG was taken at rest in all the patients to detect any evidence of ischemic heart disease. Only patients with normal resting and post-exercise ECG was included in our study.

The various tests were performed to assess the cardiovascular responses to autonomic nerve functions in patients of Irritable Bowel Syndrome and control group. The following tests were carried out:

(i) Heart rate response to Valsalva manoeuvre [9, 10]
(ii) Immediate heart rate response to standing [11 - 13]
(iii) Beat to beat variation of heart rate to single deep breath [14, 15]
(iv) Isometric hand-grip test [16]
(v) Blood pressure response to standing [17].

Result: Table 1: Showing age and sex distribution in control group and patients of irritable bowel syndrome.

Control Group			
Age in Years	**Male**	**Female**	**Total (%)**
20 - 30	8	2	10 (33.33%)
30 - 40	9	4	13 (43.33%)
40 - 50	2	2	04 (13.33%)
50 - 60	0	1	01 (3.33%)
Above 60	2	0	02 (6.67%)
Total	21 (70%)	09 (30%)	30 (100%)
Irritable Bowel Syndrome Patients			
Age in Years	**Male**	**Female**	**Total (%)**
20 - 30	08	1	09 (30.00%)
30 - 40	10	4	14 (46.67%)
40 - 50	02	1	03 (10.00%)
50 - 60	00	1	01 (3.33%)
Above 60	03	0	03 (10.00%)
Total	23 (77%)	07 (23%)	30 (100%)

Table 2: Showing frequency of various symptoms concerning GIT in Irritable Bowel Syndrome Patients compared with control group.

Symptom	**No. of IBS Patients (%)**	**No. of Controls (%)**
Change bowel pattern	30 (100%)	NIL
Diarrhoea/normal stool	06 (20%)	NIL
Diarrhoea/Constipation	10 (33%)	NIL
Constipation/Normal stool	14 (47%)	NIL
Gastrocolonic Reflex	27 (90%)	NIL
Soft stools	16 (53%)	NIL
Hard stools	14 (47%)	NIL
Borborygmi	16 (53%)	7 (23%)
Pain abdomen	24 (80%)	2 (7%)
Distension of abdomen	14 (47%)	4 (13%)
Sense of incomplete evacuation	15 (50%)	NIL
Mucus in stools	15 (50%)	NIL
Flatus	10 (33%)	4 (13%)

Onset of pain abdomen with stress	10 (33%)	NIL

Table 3: Showing distribution of Irritable Bowel Syndrome Patients in various groups.

Group	Male	Female	Total (%)
Spastic Colon	12	2	14 (47%)
Painless diarrhoea	03	3	06 (20%)
Alternating diarrhoea & constipation	08	2	10 (33%)
Total	23	07	30 (100%)

Table 4: Showing distribution of IBS Patients according to duration of disease.

Duration of the disease	Total (%)
3 months to 1 year	09 (30%)
1 year to 5 years	13 (43%)
5 years and above	08 (27%)
Total	30 (100%)

Table 5: Showing Comparison of various test among control group and Irritable Bowel Syndrome Patients and sub-groups of Irritable Bowel Syndrome.

Valsalva Ratio					
	Number Of Cases	**Mean**	**S.D**	**t**	**P**
Control	30	1.78	0.362		
T.P	30	1.84	0.498	0.568	> 0.1
Control	30	1.78	0.362		
S.C	14	1.94	0.579	1.090	> 0.1
Control	30	1.78	0.362		
P.D	06	1.65	0.319	0.795	> 0.1
Control	30	1.78	0.362		
A.D & C	10	1.82	0.421	0.282	> 0.1
Immediate Heart Rate Response to Standing					
	Number Of Cases	**Mean**	**S.D**	**t**	**P**
Control	30	1.27	0.164		
T.P	30	1.28	0.165	0.231	>0.1
Control	30	1.27	0.164		
S.C	14	1.25	0.139	0.160	>0.1
Control	30	1.27	0.164		
P.D	06	1.28	0.159	0.133	>0.1
Control	30	1.27	0.164		
A.D & C	10	1.32	0.193	0.177	>0.1
Heart Rate variation to Single Deep Breath					
	Number Of Cases	**Mean**	**S.D**	**t**	**P**
Control	30	19.6	12.04		
T.P	30	20.9	13.34	0.389	>0.1
Control	30	19.6	12.04		
S.C	14	16.93	10.64	0.693	>0.1
Control	30	19.6	12.04		
P.D	06	28.83	15.94	0.570	>0.1
Control	30	19.6	12.04		
A.D & C	10	21.7	12.83	0.457	>0.1

T.P: Total Patients, S.C: Spastic Colon, P.D: Painless Diarrhoea, A. D & C: Alternating Diarrhoea and Constipation.

Table 6: Showing Comparison of various test among control group and Irritable Bowel Syndrome Patients and sub-groups of Irritable Bowel Syndrome.

Hand Grip Test					
	Number Of Cases	**Mean**	**S.D**	**t**	**P**
Control	30	21.66	10.25		
T.P	30	20.86	06.94	0.347	> 0.1
Control	30	21.66	10.25		
S.C	14	20.43	04.35	0.421	> 0.1
Control	30	21.66	10.25		
P.D	06	20.33	10.67	0.280	> 0.1
Control	30	21.66	10.25		
A.D & C	10	21.80	07.21	0.038	> 0.1
Blood pressure response to Standing					
	Number Of Cases	**Mean**	**S.D**	**t**	**P**
Control	30	02.40	4.393		
T.P	30	03.86	3.537	1.394	> 0.1
Control	30	02.40	4.393		
S.C	14	03.57	3.478	0.856	> 0.1
Control	30	02.40	4.393		

P.D	06	03.33	3.415	0.476	> 0.1
Control	30	02.40	4.393		
A.D & C	10	04.60	3.583	1.396	> 0.1

T.P: Total Patients, S.C: Spastic Colon, P.D: Painless Diarrhoea, A. D & C: Alternating Diarrhoea and Constipation.

Discussion: This study was undertaken to evaluate autonomic nerve functions by means of cardiovascular reflexes in thirty patients of irritable bowel syndrome. Thirty normal controls, closely matched for age and sex were studied for comparison Table 1. Frequency of various symptoms concerning GIT in Irritable Bowel Syndrome patients compared with control group were shown in Table 2. Various signs of autonomic neuropathy like impotence, nocturnal diarrhoea, postural hypotension, hypertension, incontinence or retention of urine were not present in irritable bowel syndrome patients in our study. However other symptoms of autonomic neuropathy like excessive sweating and tachycardia were almost equally present among irritable bowel syndrome patients and control group. Tachycardia was present in 02 (6.6%) cases in irritable bowel syndrome group and in 03 (10%) cases in control group. Excessive sweating was present in 02 (6.6%) cases in irritable bowel syndrome group and in none in control group. Symptoms which may be attributed to autonomic irritability such as palpitations 12 (40%), cold hands 10 (33.3%), anorexia 07 (23.3%), faintness and weakness 04 (13.3%) and belching 03 (10%) were present with almost equal frequency in various subgroups of irritable bowel syndrome patient. Frequency of these symptoms was more in irritable bowel syndrome patients than in control group. In control group, palpitations were observed in 03 (10%),
belching 02 (6.6%), cold hands 01 (3.3%) cases, while anorexia, faintness, weakness and flushing were present in none. All the above mentioned symptoms attributed to autonomic irritability and autonomic neuropathy might well be present in anxiety. Incidence of anxiety had been reported to be higher in irritable bowel syndrome patients than in normal population [18 – 24].Therefore, the so called symptoms of autonomic irritability and autonomic neuropathy are well be due to high incidence of anxiety and tension states present in irritable bowel syndrome patients as observed by different workers.

The incidence of anxiety in irritable bowel syndrome patients in our study was not evaluated as this requires a separate study on all associated psychiatric illnesses in irritable bowel syndrome patients including anxiety and tension.

Table 5 and Table 6 shows the comparison among control group and patient of irritable bowel syndrome to find whether there is any statistical significance. The first three tests that is heart rate response to Valsalva manoeuvre, immediate heart rate response to standing, beat to beat variation of heart rate to single deep breath are meant for assessing the integrity of parasympathetic innervation, and last two tests that is isometric hand-grip test, blood pressure response to standing are to evaluate sympathetic innervation of heart. The lower limit of normal Valsalva manoeuvre ratio in our study was 1.11 in control group which is in accordance with values observed by Ewing et al [9]. For interpreting the significance of
Valsalva manoeuvre ratio, we took 1.11 or greater as normal response in irritable bowel syndrome patients as determined in controls of our series. The range of Valsalva manoeuvre ratio in control group in our series was 1.11 to 2.42 which is close to the range observed by Bhatia et al [10]. The mean Valsalva ratio observed in controls in our series was 1.78 ± 0.362. The range of Valsalva ratio observed in irritable bowel syndrome patients in our series was 1.12 to 3.00 and mean Valsalva ratio 1.84 ± 0.498 and the difference was statistically insignificant (P>0.1). Also, duration of the irritable bowel syndrome did not affect the Valsalva ratio in comparison to normal controls (P>0.1). By Valsalva manoeuvre, cardiac dysautonomia was not detected in any patient of irritable bowel syndrome or in any subgroup of irritable bowel syndrome patients.

Immediate heart rate response to standing the method used is same as that of Maisey [12] lower limit of maximum heart rate: minimum heart rate ratio in control group was 1.05. The range of the results observed in control group was 1.05 to 1.66 and in irritable bowel syndrome group it was 1.11 to 1.77. The mean ratio in control group was 1.27 ± 0.164

and in irritable bowel syndrome group 1.28 ± 0.165 and it is statistically not different (P>0.1). Duration of the irritable bowel syndrome did not impair the response (P>0.1). Response was normal in irritable bowel syndrome patients as a whole and in various subgroups of irritable bowel syndrome patients as well.

Beat to beat variation of heart rate to single deep breath [14, 15] in our series the range of the difference of heart rate between maximum and minimum R-R interval after single deep breath in controls was 4 to 47 beats/minute. In control group, the mean difference of heart rate between maximum and minimum R-R interval during single deep breath was 19.6 ± 12.04 beats/minute. In irritable bowel syndrome group the range of the difference of heart rate between maximum and minimum R-R interval after single deep breath was 5 to 54 beats/minute and mean difference was 20.9 ± 13.34 beats/minute. However there was no statistically significant difference between values observed in control group and irritable bowel syndrome group and its subgroup (P>0.1). Duration of the disease did not affect the response in irritable bowel syndrome patients in comparison to normal controls (P>0.1).

Isometric hand-grip test in our study the range of rise in diastolic blood pressure in response to sustained hand-grip at 30% of the maximum voluntary contraction was 10 to 48 mm Hg in controls. The mean increase in diastolic blood pressure in controls was 21.66 ± 10.25 mmHg. The lower limit of normal value observed as 10 mmHg in our series in control group is in accordance with value noted by Ewing [16]. The range of rise in diastolic blood pressure in irritable bowel syndrome patients was 10 to 42 mm Hg and mean increase in diastolic blood pressure was 20.86 ± 6.94 mm Hg. Statistically there was no significant difference between controls and irritable bowel syndrome patients in response to sustained hand-grip test (P>0.1) and between controls and different subgroups of irritable bowel syndrome patients. Duration of disease exhibited a normal response in comparison to controls (P>0.1).

Blood pressure response to standing [17] in our study the change in systolic blood pressure on standing observed in control group in our series ranged from fall of 10 mm Hg and its mean was 2.4 ± 4.39 mm Hg. In irritable bowel syndrome group range of change in blood pressure was from 10 mm Hg fall to 2 mm Hg rise with a mean of 3.86 ± 3.53 mmHg. There was no statistically significant difference between the values of this test obtained in the control group and irritable bowel syndrome group (P>0.1) and its subgroups. The response was normal in irritable bowel syndrome patients grouped according to duration of disease (P>0.1).

No abnormality was found in cardiovascular responses to any of the above five tests between subjects below and those above 40 years of age in control as well as irritable bowel syndrome groups.

Conclusion: There was no evidence of autonomic (sympathetic and parasympathetic) neuropathy in irritable bowel syndrome patients in either sex or in their various subgroups as evaluated by testing cardiovascular reflexes in them. No impairment of the cardiovascular response to various autonomic tests was present with increasing duration of disease or with advancing age in irritable bowel syndrome patients.

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