ISSN 0976 – 3333

Available Online at www.ijpba.info

International Journal of Pharmaceutical & Biological Archives 2013; 4(5): 968 - 972

ORIGINAL RESEARCH ARTICLE

Existence of Oesophageal Dysmotility and Autonomic Dysfunction in Patients with Gastrointestinal Symptoms – An Analysis

Dr. R. Tharakeswari*

Associate professor, Department of Physiology, Karuna Medical College, Chittoor, Palakkad, Kerala, India

Received 06 Jul 2013; Revised 09 Oct 2013; Accepted 18 Oct 2013

ABSTRACT

Aim - Damage in the extrinsic nerve supply to the gut can manifest as GI motility disorders. Both sympathetic and parasympathetic or may be disturbed. Hence autonomic dysfunction has an impact on the GI motility function and progresses as functional gut disorders. Different opinion prevails on the prevalence rate of the autonomic damage in patients with GI dysmotility.

Study design - 34 patients who presented with upper GI symptoms relating to functional disorders were subjected to the manometry test. On the same patients the autonomic function tests were performed to test for sympathetic and parasympathetic activity of ANS to study the extent of autonomic damage.

Results - Among patients subjected to manometry, 83% of them with GI symptoms showed dysmotility pattern. Those who were symptomatic underwent the autonomic function tests, out of which 49.3% of them showed an abnormal autonomic function. Statistical analysis was done using Fisher's exact test between the two groups and that showed a significant difference (p=0.0476).

Conclusion - In this study, a definite autonomic damage in 49.3% of patients has been observed. The tool can be used along with GI manometry and it is also a non invasive tool. The test contributes in identifying the autonomic involvement of the digestive tract and hence identifying the gut symptoms when motility studies are not available or contra-indicated. Hence performing this test on patients with GI symptoms along with manometry shall facilitate us to assess the extent of autonomic damage for better diagnosis and further treatment.

Key words: Dysphagia, noncardiac chest pain, regurgitation, autonomic dysfunction.

INTRODUCTION

Symptoms due to malfunction of upper gastrointestinal segment are numerous, to name some are retrosternal chest pain very often confused by the patients as cardiac pain. We call it as non-cardiac chest pain, dysphagia which is difficulty in swallowing to liquids, solids or even both. Another common encounter would be regurgitation.

Damage in the extrinsic nerve supply to the gut can manifest as GI motility disorders. Sympathetic and parasympathetic or both may be disturbed. Hence autonomic dysfunction has an impact on the GI motility function and progresses as functional gut disorders. Vagal dysfunction has been implicated as a prime etiological factor for peristaltic abnormalities and also spastic activity of patients with GI symptoms [1].

Different opinion prevails on the prevalence rate of the autonomic damage in patients with GI dysmotility.

The aim of the study is to assess the type and distribution of the oesophageal motility disorders along with prevalence of autonomic dysfunction using the standard autonomic function tests on patients with GI symptoms. The patients underwent GI manometry a diagnostic procedure which gives the details of oesophageal motility pattern, lower oesophageal sphincter pressure and the receptiveness of the sphincter to the oesophageal peristalsis. The same patients were subjected to the autonomic function tests.

A.E. Bharucha [2] reported as the prevalence of abnormal autonomic function to be 29 % in patients with upper GI dysmotility. A. Pirtniecks

***Corresponding Author:** Dr .R. Tharakeswari, **Email:** drtharakeswari@gmail.com

[3] in their study have said that 40 % of patients with Non specific disorders of oesophageal motility have significant abnormalities of Vagal function. In 2002 Sonia Letcia [4] using the HRV response analysis have interpreted autonomic damage in patients with GI dysmotility – dyspepsia using both time and frequency domain indicies. The projection was 30.4 % of them had abnormal Vagal function (Parasympathetic damage).

MATERIALS AND METHODS

All patients who presented with GI symptoms like non cardiac chest pain, dysphagia and regurgitation were taken up for the study. A prospective controlled study was done and all patients were subjected to oesophageal manometry and autonomic function tests. The sample size was 34. Written consent for investigation was obtained in all cases and the study approved by the hospital Ethics Committee.

INCLUSION CRITERIA:

1) Age groups of 20 to 50 years
2) Both Men and women were included
3) Only patients with upper GI symptoms like retrosternal pain ie non cardiac chest pain, dysphagia, regurgitation were included in the study.

EXCLUSION CRITERIA:

1) Age group <20 and >50 not included
2) Patients with associated systemic disease like connective tissue disorders. eg: Scleroderma
3) Subjects on drugs that would cause autonomic damage were not included.
4) Persons with diabetes mellitus were excluded, as it would confound the interpretation of autonomic function test.

Patients who presented with upper GI symptoms relating to functional disorders were subjected to the manometry test. Oesophageal manometry was performed by the station pull-through technique. The transducer probe has sensors at 5cm intervals. The test was done using eight channel catheter by water perfusion technique using the machine Red Tech Inc, model 2000 GiPc Motility system. Peristaltic activity in response to ten wet swallows to record the oesophageal motility pattern was used and the lower oesophageal sphincter pressure was recorded. Sphincter response to the swallows was also noted. The test was performed and diagnosed by standard criteria's (castell and castell) [5] taking into consideration the oesophageal motility parameters and LES sphincter pressure.

A non-specific oesophageal motility disorder was manometrically defined as abnormal motility including one or more of the following criteria:

1. increased non-transmitted contractions (≫20% wet swallows);
2. prolonged duration of peristaltic waves (≫6 s);
3. retrograde contractions;
4. multiple/triple peaked contractions;
5. low amplitude swallow waves (≪30 mmHg)/synchronous activity;
6. isolated incomplete lower oesophageal sphincter relaxation (residual pressure 0.8 mmHg).

Also all the patients and controls were subjected to seven standard autonomic function tests for both parasympathetic and sympathetic function assessment. All the tests were non- invasive, very simple and easy for patients to understand and perform it. The tests were performed 2 hours after meals and they were instructed to avoid caffeine beverages at least 2 hours before test and not to consume alcohol 24 hours prior to the study.

The tests were carried out in the equipment BIOPAC SYSTEM. The instrument is "BIOPAC SYSTEMS, Inc." MANBSL3S student/bookstore version, it includes the biopac systems MP 30 hardware unit, customized and configured with biopac student labpro software. The ECG recordings were done with this and computerized values were obtained. The blood pressure recordings were done using the sphygmomanometer.

The tests done were as follows;

1) Heart rate variation during deep breathing.
2) Heart rate response to Valsalva manoeuvre.
3) Heart rate increase to standing.
4) 30: 15 ratio. (RR interval).
5) Blood pressure response to standing.
6) Sustained hand grip test.
7) Cold pressor test.

Out of the above mentioned tests, the first four are to evaluate the parasympathetic function and the last three are to evaluate the sympathetic function.

TESTS REFLECTING PARASYMPATHETIC DAMAGE

1. **HEART RATE VARIATION DURING DEEP BREATHING:**

The subject was asked to breathe deeply at six breaths / min (five seconds 'in' and five seconds 'out') for one minute. An ECG was recorded throughout the period of deep breathing and onset of inspiration and expiration was marked in the monitor and the recording was obtained. The maximum and minimum heart rate during each breathing cycle was obtained from the recordings and the data obtained. The result of the test was expressed as the mean of the difference between the maximum and minimum heart rates for six cycles in beats/min. The normal score would be = 10 or > 15 beats / min. A value of < 10 beats / min is pathological.

2. HEART RATE RESPONSE TO VALSALVA MANOEUVRE:

The subject was made to lie in supine position and then asked to blow into a mouth piece attached to a manometer, holding it at a pressure of 40 mm Hg for 15 seconds and a continuous electrocardiogram (ECG) was recorded. Due care was taken to prevent deep breathing before and after the release of strain. ECG was continued to record after the release. The valsalva ratio was calculated as

$$\frac{\textbf{Longest RR interval after the manoeuvre}}{\textbf{Shortest RR interval after the manoeuvre}}$$

The normal is > 1.45.

3. HEART RATE INCREASE TO STANDING:

The test was performed with the subject lying quietly in a couch while the heart rate was recorded in a continuous ECG monitor. The patient was asked to stand unaided and the point at starting to stand was marked on the monitor. The heart rate at the peak acceleration was noted from the monitor. The difference between the heart rate at the peak acceleration on standing and the resting level gives an indication of the increase in heart rate. The normal is, there would be an increase of heart rate up to 20 beats at the peak acceleration.

4. 30: 15 Ratio

The ECG was recorded continuously as the subject was lying and was asked to stand and the recording was continued. The shortest RR interval at or around the 15^{th} beat and the longest RR interval at or around the 30^{th} beat after starting to stand was measured from the recorded ECG. The ratio is calculated.

The normal would be> 1.04.

TESTS REFLECTING SYMPATHETIC DAMAGE

5. BLOOD PRESSURE RESPONSE TO STANDING

In this test the subject's blood pressure is measured with a sphygmomanometer while lying supine and immediately after he was made to stand up. The recording was done three times and the mean was calculated. The postural fall in blood pressure was taken as the difference between the systolic pressure in lying and the systolic pressure in standing posture. The normal systolic fall would be up to < 10 mm Hg.

6. BLOOD PRESSURE RESPONSE TO SUSTAINED HAND GRIP.

The patient was asked to grip the handgrip dynamometer and apply maximum pressure with their dominant hand. 30% of their voluntary capacity was obtained. The patient was asked to maintain a sustained grip at that 30% of capacity for 3 minutes. 3 recordings of blood pressure were done at 1 minute interval. The blood pressure taken just before release of hand grip is most essential. The result is expressed as highest diastolic blood pressure during hand grip. The normal would be a rise in diastolic pressure of > 15 mm Hg.

7. COLD PRESSOR TEST

This test was evaluated by immersion of subject's left hand (up to) wrist in cold water at 4 ' C for 1 minute, in recumbent state. Blood pressure was measured during immersion of hand and on removal of hand. The normal would be an increase in diastolic pressure up to 10 mm Hg.

Interpretation of the test was based on the works of Ewing and Clarke.

Table 1: Interpretation of autonomic function tests

Test	Normal	Borderline	Abnormal
Heart rate variation	> 15	11 – 14	< 10
Valsalva ratio	> 1.21	1.11 – 1.20	< 1.10
Heart rate increase to standing	> 20	19 – 13	< 12
30 : 15 Ratio	> 1.04	1.01 – 1.03	< 1.00
BP response to standing	< 10	11 – 29	< 30
BP response to hand grip	> 16	11 – 15	< 10
Cold pressor test	> 10	8 – 10	< 8

The individual autonomic function score was determined for every subject.

Based on these scores the patients were categorized as normal or with autonomic dysfunction. The distribution of autonomic damage in individual oesophageal motility disorder was looked for.

RESULTS

Among patients subjected to manometry, 83% of them with GI symptoms showed dysmotility pattern.

Table 2: The type and distribution of oesophageal motility disorder

S. No	Oesophageal motility disorder	Percentage of distribution
1	Diffuse oesophageal spasm	28.4%
2	Achalasia cardia	27.5%
3	Reflux disease	22.5%
4	Nutcracker oesophagus	5.1%
5	Hypertensive Lower Oesophageal Sphincter(LES)	16.5%

Those who were subjected manometry test also underwent the tests for autonomic function out of which 49.3% of them showed an abnormal autonomic function. Out of which only 5% showed severe autonomic damage where the presentation was presence of both parasympathetic and sympathetic damage. None of the patients had sympathetic damage alone. The extent of damage in each motility disorder was looked which showed a pattern as shown in (**Fig 1**).

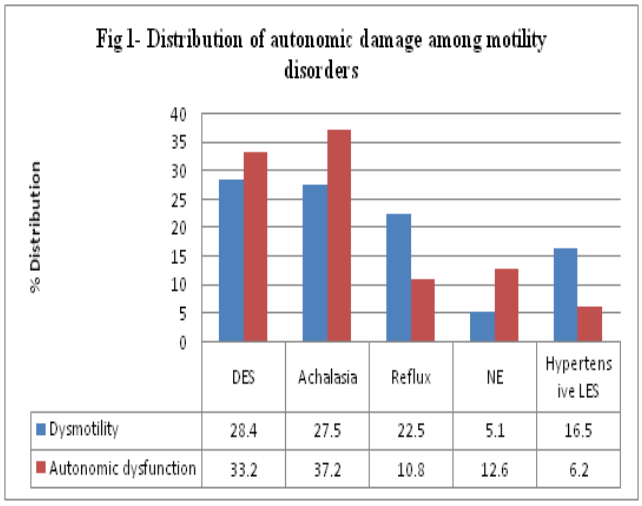

Fig 1: Distribution of autonomic damage among motility disorders

Statistical analysis was done using Fisher's exact test between the two tests that was performed on patients and that showed a significant difference (p=0.0476).

DISCUSSION

Pirtniecks has said that denervation is an important factor in etiology of motility disorder. Diffuse esophageal spasm and nut cracker esophagus have been reported to evolve into achalasia which is common pattern in motility disturbance. Also he has projected an autonomic damage of 40 % in patients with esophageal dysmotility.

Sonia Leticia has mentioned that the extent of vagal damage implies impaired functioning and hence this plays a major role in pathogenesis of the diseases. They have reported a damage of 30.4 %. Bharucha has reported in their study as autonomic dysfunction is frequent in patients with symptoms suggestive of GI dysmotility when a neurological diagnosis is identifiable, who has reported an autonomic damage of 29 % in patients with upper GI dysmotility and 69 % in patients with diabetes and dysmotility. Autonomic dysfunction can be also get augmented due to many other medical conditions like diabetes mellitus which if also present can worsen the situation [6]. We need to also remember other non gastrointestinal causes like sleep apnoea, cardiac failure which can also if associated can hasten the damage [7]. Motility disorders like diffuse oesophageal spasm, Achalasia cardia, Nutcracker oesophagus, hypertensive lower oesophageal sphincter have no specific aetiology or pathology. They are diagnosed clinically on the manometry recording findings (**Table 3**).

Impairment of oesophageal innervations can also cause delay in oesophageal clearance and also gastric emptying. Enteric nervous system unique to GIT if damaged can cause achalasia, Diffuse oesophageal spasm the pathology mainly in the Auerbach's plexus [8,9]. Nut cracker oesophagus can eventually present as Achalasia [10,11].

Different motility disorders can present with different degree of autonomic damage which is well appreciated in this study. In this study we have noticed a definite autonomic damage in 49.3% of patients. The tool can be used along with GI manometry and it is also a non invasive tool. The test contributes in identifying the autonomic involvement of the digestive tract and hence identifying the gut symptoms when motility studies are not available or contra-indicated.

Table 3: Criteria used to diagnose primary oesophageal motility disorder

Type of motility disorder	Manometric criteria
Achalasia oesophageal	Absent peristalsis in oesophageal body with/without incomplete lower sphincter relaxation, or a hypertensive lower oesophageal sphincter
Diffuse oesophageal spasm	Simultaneous contractions in >/= 20% of wet swallows, with/without repetitive/prolonged/high-amplitude contractions, or lower oesophageal sphincter abnormalities (incomplete relaxation and high resting pressure)
Nutcracker oesophagus	Peristaltic waves of high amplitude (mean > 180 mmHg)
Hypertensive lower oesophageal sphincter	Resting pressure > 45 mmHg

Hypotensive lower oesophageal sphincter	Resting pressure < 10 mmHg
Ineffective peristalsis	Low-amplitude contractions (< 30 mmHg) in 30% or more of wet swallows
Non-specific oesophageal motility disorder	Any combination of the following:
	non-transmitted contractions in >/= 20% of swallows
	triple picked contractions
	retrograde contractions
	isolated, incomplete lower oesophageal sphincter relaxation
	Prolonged-duration peristaltic waves (> 6 s)

Adapted from Castell and Castell.

Hence performing this test on patients with GI symptoms along with manometry shall facilitate us to assess the extent of vagal damage for better diagnosis and further treatment. The enteric nervous system and its changes after damage to oesophagus causing disorder is a versatile area for exploration as not much of studies have been reported in this [12,13].

CONCLUSION

Assessing autonomic function in patients with oesophageal motility disorders along with oesophageal manometry will help in detecting and classifying the motility disorders.

The tests done in this study to assess the autonomic function are very simple, non invasive, less expensive and will be available even at primary health centers. There are also computerized systems which makes analysis even more simple [14]. Hence these tests can be used as a routine along with manometry as it contributes to the identification of motility disorder. Also it can contribute significantly in diagnosis of patients with identified upper GI symptoms when manometry is not available or contraindicated.

REFERENCES

1. Heatley R.V., Collins R.J., James P.D., At kinson M. Vagal function in relation to gastroesophageal reflux and associated motility changes. Br Med J 1980; 280:755-757.
2. Bharucha AE, Camilleri M, Low PA. Autonomic dysfunction in gastrointestinal motility disorders. Gut 1993; 34:397-401.
3. Pirtniecks A, Smith LF, Thorpe JAC. Autonomic dysfunction in non-specific disorders of oesophageal motility.
4. Sonia Leticia silva lorena, Marco jansen de oliveira figueiredo. Autonomic function in patients with functional dyspepsia assessed by 24 hr Heart rate variability. Digestive diseases and sciences 2002; 47:27-31.
5. Katz P.O., Castell D.O. Review: esophageal motility disorders. Am J Med Sci1985; 290(2):61-68.
7. Walker S.J. What's new in pathology, pathophysiology and conservative treatment of benign oesophageal disorders. Dis Oesophagus 1997; 10:149-154.
8. Thorpe J.A.C., Edward C., Thompson R., Mathews H.R. Histology and immunofluorescence of oesophageal muscles in achalasia. Diseases of the esophagus. London: Springer Verlag; 1987. p. 928.
9. Vantrappen G., Janssens H., Hellemans T. Achalasia: DOS and related motility disorders. Gastroenterology 1979; 76:450-457.
10. Paterson W.G., Beck I.T., DaCosta L.R. Tr ansition from Nutcracker esophagus to achalasia. J Clin Gastroenterol 1991; 13(5):554-558.
11. Knight G.C. The relationship of the extrinsic nerves to the functional activity of the oesophagus. Br J Surg 1934; 22:155-168.
12. O'Hanrahan T., Bancewicz J., Thomson D. , Marples M., Williams D. Oesophageal reflex responses: abnormalities of the enteric nervous system in patients with oesophageal symptoms. Br J Surg 1992; 79(9):938-941.
13. Tougas G., Hunt R.H., Fitzpatrick D., Upt on A.R. Evidence of impaired afferent vagal function in patients with diabetic gastroparesis. Pacing Clin Electrophysiol 1992; 15(10):1597-1602.
14. Low PA, Laboratory evaluation of autonomic failure. In: Clinical autonomic disorders– evaluation and management 2nd ed, New York: Lippincott-Raven, 1997. p. 179.
15. Greenwood J.P., Batin P.D., Nolan J. Clinical application of cardiac autonomic assessment. Br J Cardiol 1997; 4(5):183-187.