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Original Research Article

Cardiovascular response to sustained handgrip test in gastroesophageal reflux disease patients

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ABSTRACT

Background: Gastroesophageal reflux disease pathogenesis may be associated with disturbances of the autonomic nervous system.
Methods: One hundred five participants aged 35-45 years of either sex, which include Gastroesophageal reflux disease patients, thirty five each (who presented typical symptom of Gastroesophageal reflux disease with reflux esophagitis (ERD) and without reflux esophagitis (NERD)) and thirty five age and sex matched control subjects, were enrolled in the study. Autonomic function test was assessed using Sustained Handgrip test.
Results: In the present study, no significant difference was observed in age, height, weight, body mass index, resting systolic blood pressure and diastolic blood pressure between the study groups. The mean difference of diastolic blood pressure (mmHg) response to Sustained Handgrip test between ERD and NERD; ERD and Control; NERD and Control was statistically highly significant ($p=0.001$; $p<0.001$; $p=0.029$, respectively), predicting reduced sympathetic activity in gastroesophageal reflux disease, more in patients with reflux esophagitis (ERD).
Conclusions: Reduced sympathetic activity can cause impairment of lower esophageal sphincter function, particularly of the neural mechanisms related to control of transient lower esophageal sphincter relaxation. It might increase number and time duration of transient lower esophageal sphincter relaxations resulting in pathological enhancement of GERD.

Keywords: Autonomic nervous system, Gastroesophageal reflux disease, Sustained handgrip test

INTRODUCTION

Gastroesophageal reflux disease (GERD) is a condition that develops when the reflux of stomach contents causes troublesome symptoms and/or complications.[1] GERD is a highly prevalent gastrointestinal (GI) disorder, affecting the upper part of the gastrointestinal tract, and is one of the most common GI illnesses encountered in clinical practice. The incidence and prevalence of GERD are rising, it is estimated to affect 10 – 20% of the inhabitants of Western countries and 5% of Asians.[2] A cross sectional study reported prevalence rate for reflux symptoms of 7.5% in Indians, 0.8% in Chinese and 3% in Malays.[3] The two previous Indian studies gave a weekly prevalence of GERD symptoms inthe range of 22–25%.[4,5]

GERD is usually divided into two main subclasses, with mucosal inflammatory changes (esophagitis) (ERD - Erosive Reflux Disease) and without mucosal inflammatory changes (NERD - Non Erosive Reflux Disease).[6]

The most important mechanism causing gastroesophageal reflux is the transient lower esophageal sphincter

relaxations (TLESRs). In GERD patients a higher percentage of TLESRs is accompanied by reflux.[7]

GERD pathogenesis may be associated with disturbances of the autonomic nervous system (ANS).[8] Gastroesophageal reflux may not be mediated solely through parasympathetic activity but also involve sympathetic activity. Therefore the present research included Sustained handgrip test to assess the sympathetic activity of autonomic nervous system in GERD patients.

The Sustained handgrip test is a useful measure of autonomic damage and when abnormal, implies extensive damage to sympathetic efferent pathways. It is the only single measure of reflex sympathetic damage test available, which fulfils the criteria for a useful test of autonomic function.[9]

Thus, the aim of the present study was to assess cardiovascular autonomic neuropathy in GERD patients by using Sustained Handgrip test.

METHODS

The present study was carried out in the Upgraded Department of Physiology, S.M.S. Medical College with requisite collaboration from the Department of Gastroenterology, S.M.S. Hospital, Jaipur. The study was carried out after getting formal approval from institutional ethics committee of S.M.S. Medical College, Jaipur.

The clinical assessment for the GERD was done by gastroenterologist using standard clinical protocol. Subjects having clinical symptoms of GERD were subjected to Endoscopic examination of upper gastrointestinal tract for the assessment of esophageal mucosa in Department of Gastroenterology, S.M.S. Hospital, Jaipur. Informed written consent was obtained from all the subjects prior to study.

One hundred five participants, aged 35-45 years of either sex were enrolled in the present research, which were grouped as follows:

- GERD patients with reflux esophagitis (ERD; n=35)
- GERD patients without reflux esophagitis (NERD; n=35)
- Healthy Control subjects (Control; n=35)

Exclusion criteria for ERD, NERD and Controls was: Any acute or chronic illness, subjects taking any medication that modulate Autonomic Nervous System activity and affect gastrointestinal motility and/or gastric acid secretion, alcoholic, smokers, tobacco chewers, stress, psychotic or demential disorders, obese and non-cooperative subjects. The control subject who have suffered from any upper GI tract disease, were also excluded.

The study protocol was explained to subjects before start of procedure. A detailed history regarding age, sex, height, weight, body mass index (BMI), alcoholic, smokers, tobacco chewers and resting blood pressure were taken and physical examination was done. Autonomic evaluation was carried out in the morning from 10:00 to 12:00 noon, 2 hour after a light breakfast and after familiarizing the subjects with the test procedures.

Sustained handgrip test (SHT)

The maximal isometric contraction ($T_{max.}$) was first measured by asking the subject to hold the hand dynamometer in right hand (or dominant hand) to have a full grip as hard as possible for a few seconds and then to maintain handgrip steadily at 30 percent of that $T_{max.}$ for as long as possible up to a maximum of five minutes. Blood pressurewas measured with sphygmomanometer on the non-exercising arm. The blood pressureresponse to Sustained Handgrip test was expressed as the diastolic blood pressure (DBP) just before release of handgrip. This parameter indicated cardiac sympathetic response.

The index of DBP response to the Sustained Handgrip test was taken as the difference between the DBP just before release of handgrip and the mean of three resting DBP readings. The change in mean DBP in response to sustained handgrip test was interpreted as:[10]

- ≥ 16 mmHg was taken as normal
- 11 -15 mmHg as Borderline
- ≤ 10 mmHg as Abnormal.

Statistical analysis

Data were presented as mean and Standard Error (mean±SE). Statistical analysis was performed by using one way ANOVA (Bonferroni) test for comparisons of DBP response to Sustained Handgrip test between the study groups. The data was analyzed with the use of Microsoft Excel 2007 and SPSS for windows, version 16.0 (Chicago, SPSS Inc., 2007). A p value <0.05 was considered significant at 95 % Confident Interval.

RESULTS

Table 1 depicts the demographic data, blood pressure and DBP (mmHg) response to Sustained Handgrip test of study groups. No significant difference was observed in age, height, weight, body mass index, resting SBP and resting DBP between the study groups, whereas DBP response to SHT shows a statistical highly significant difference ($p<0.001$) among the three study groups by one way ANOVA.

Table 1: Demographic data and DBP response to sustained handgrip test of studied groups.

Parameters	ERD (n=35)	NERD (n=35)	Control (n=35)	ANOVA p value
Age (years)	38.86±0.50	39.57±0.69	39.29±0.67	0.719†
Height (cm)	168.46±1.05	164.00 ±1.61	163.60 ±2.00	0.063†
Weight (kg)	62.31±1.70	60.77±2.00	63.17±1.57	0.624†
BMI (kg/m^2)	22.03±0.63	22.59±0.68	23.55±0.36	0.172†
Resting SBP (mmHg)	117.37±2.06	118.54±2.01	120.03±2.01	0.650†
Resting DBP (mmHg)	73.69±1.32	74.26±1.30	76.03±1.82	0.517†
DBP(mmHg) response to SHT	5.43±0.45	10.03±0.80	13.14±1.12	0.000*

Values are mean±SE, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SHT: Sustained handgrip test, †p>0.05 [Nonsignificant], *p<0.05 [Significant].

After applying Post hoc test, Bonferroni (Figure 1), it was observed that the mean difference of DBP (mmHg) response to Sustained Handgrip test between ERD and NERD; ERD and Control; NERD and Control, was statistically highly significant (p=0.001; p<0.001; p=0.029, respectively).

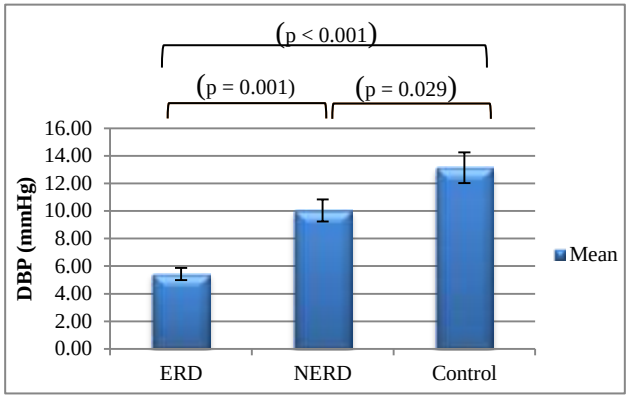

Figure 1: Comparison of mean±SE and post hoc test, Bonferroni values of DBP (mmHg) response to sustained Handgrip test (SHT) among the studied groups.

Table 2 shows the range of DBP response to Sustained Handgrip test (SHT) in the study groups. Thirty three subjects of ERD and twenty three subjects of NERD out of thirty five subjects each had less than 10 mmHg DBP response to Sustained Handgrip test that indicates sympathetic insufficiency in GERD patients, more in ERD.

Table 2: Range of DBP response to sustained Handgrip test (SHT) in the studied groups.

DBP (mmHg)	Number of subjects		
	ERD (n=35)	NERD (n=35)	Control (n=35)
≤10	33	23	12
11- 15	1	9	14
≥16	1	3	9

DISCUSSION

Gastroesophageal reflux disease (GERD) is defined by the presence of esophageal mucosal breaks or by the occurrence of reflux-induced symptoms which are severe enough to impair the quality of life.[11]Autonomic nervous dysfunction had frequently been observed in patients with gastroesophageal reflux diseases (GERD) and impacts the pathogenesis of GERD.[12]

Cardiovascular autonomic function tests are widely used to detect, verify and quantify the cardiovascular autonomic dysfunction. They have been tested for their validity and reliability.[13]

During Sustained Handgrip test, sympathetic cardiac efferent fibers are tested by isometric exercise.[14] Ewing reported that in sustained handgrip, there was normally a heart rate-dependent increase in cardiac output with no change in peripheral vascular resistance and a consequent increase in systemic blood pressure. The blood pressure could alternatively be increased by peripheral vasoconstriction.[15]

Chakraborty et al was the first to perform the whole set of cardiovascular reflex tests. They revealed unequivocal levidence of autonomic nervous system dysfunction in 40% of patients, although none had symptoms of autonomic failure.[16]

The present research demonstrates significant differences (p<0.001) in the DBP (mmHg) response to Sustained Handgrip test in both GERD patients with reflux esophagitis (ERD) and without reflux esophagitis (NERD) as compared to control subjects (Table 1). When intergroup comparison was done, it was observed that GERD patients with reflux esophagitis have highly significant difference in DBP (mmHg) response to Sustained Handgrip test as compared to GERD patients without reflux esophagitis and control subjects (Figure 1). Thus these findings determined that sympathetic autonomic dysfunction occurs in GERD patients, more in patients with reflux esophagitis.

The present study observed that out of thirty five subjects in each group, twenty subjects of NERD and thirty two subjects of ERD had less than 10 mmHg DBP response to Sustained Handgrip test, indicating more reduced sympathetic activity in the GERD patients than in control subjects (Table 2).

The present study shows similar findings to study done by Campo et al. They observed a significantly reduced rise of DBP in response to Sustained Handgrip test (SHT) in GERD patients with esophagitis (ERD) as compared to control subjects. A significant lower DBP response to SHT was found when ERD patients were compared with non-reflux patients (NERD).[17] However, other studies done by Elewa et al and Milovanovic et al found no significant differences in DBP response to Sustained Handgrip test in patients with GERD than in control group.[18,19]

The probable reason of the present findings is due to the decreased sympathetic activity. Reduced sympathetic activity can cause intrinsic inhibitory reflex disturbances and increased number and time duration of TLESRs episodes resulting in pathological enhancement of GERD.

The basal tone of LES is mediated by a release of acetylcholine from excitatory motorneurons. At rest the inhibitory neurons controlling the LES are inactive and become activated during LES relaxation. The sympathetic postganglionic fibers may inactivate neural circuits that generate motor activity, which permitting continuous activity in the inhibitory intrinsic motorneurons. The loss of this inhibitory control may be followed by impairment of LES function, particularly of the neural mechanisms related to TLESR control. These inhibitory motorneurons also activated by vagal fibers. The loss of this adrenergic or vagal nonadrenergic modulation may provide excessive or uncoordinated motor responses.[17]

The observed autonomic dysfunction may probably cause intrinsic inhibitory reflex disturbances, abnormal fundal accommodation and gastric emptying, and consequently an increased number of transient lower esophageal sphincter relaxations (TLESRs) resulting in GERD.[17]

CONCLUSION

The present study concluded that sympathetic activity was more reduced in ERD patients than in NERD patients when compared with control subjects. This autonomic dysfunction can be counted between the pathogenetic factors of Gastroesophageal reflux disease by increasing the numbers of TLESRs. This research identified GERD patients with reflux esophagitis (ERD) with sympathetic dysfunction and accounting for neurologic approaches and pathophysiology and treatment of GERD patients.

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