Original Article

Esophageal Motility Disorders in Diabetics with and without Neuropathy

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Abstract

Objective: To detect the presence of esophageal motor disorders in diabetic patients, and to establish whether there is any difference between patients with and without neuropathy.

Methods: Fifty-six diabetic patients admitted at Department of Medicine at Ziauddin Medical University Hospital, Karachi were selected to observe if manometeric findings were different in diabetic patients with and without diabetic neuropathy.

Results: Poor glycemic control was observed amongst patients with diabetic neuropathy as compared to those without neuropathy. Double peaked peristalsis and failure of peristalsis was more common in patients with diabetic neuropathy as compared to those without neuropathy. High amplitude and broader wave peristalsis and hypertensive lower esophageal sphincter was found in patients without neuropathy. Aperistalsis and multiple peaked waves were equally prevalent in patients with and without neuropathy.

Conclusion: Poor glycemic control was found in patients with diabetic neuropathy, double peaked and failed peristalsis was the most common manometric abnormality among them (JPMA 56:54;2006).

Introduction

Chronic gastrointestinal symptoms in association with diabetes mellitus had been recognized for a long time but it was the report by Rundles in 1945 that first drew attention to the effects of diabetes on the gut.[1] Subsequently, the gastrointestinal manifestations of diabetes have been the subject of several reviews.[2-4] Those features of neuropathies have been included in several reviews of diabetic autonomic neuropathy.[5-7] Clinical manifestations of esophageal dysfunction as a complication of diabetes are rare, although dysphagia and diffuse ulceration have been described.[8,9] Evidence for altered esophageal motor function in diabetes was first reported in 1967.[10] Esophageal motor dysfunction has been detected by cine radiographic or manometric techniques for a long time[11], but so far esophageal manometry is the gold standard for the detection of esophageal motor disorders.

It is well established that esophageal manometric abnormalities are common in diabetic patients with peripheral neuropathy.[12-14] The clinical significance of this fact is uncertain since most of these patients remain asymptomatic. The pathophysiology of these abnormalities may be due to the degenerative effects of diabetes mellitus on the autonomic nervous system, rather than smooth muscle dysfunction.[15,16] However the etiology of symptoms in these patients are poorly understood.[16] Present study was conducted to see whether the manometric abnormalities are different in patients with and without diabetic neuropathy.

Patients and Methods

Fifty-six adult patients of either gender with diabetes mellitus, admitted in Ziauddin Hospital were included in the study. In order to see the difference in the esophageal motility, half of them i.e. 28 patients were taken with diabetic neuropathy and 28 cases without neuropathy.

Peripheral neuropathy was considered to be present, if two or more of the following abnormalities were present: pain, weakness, paraesthesia, hypoaesthesias and trophic ulcers.

Autonomic neuropathy was considered by the standardized measurement of cardiovascular reflexes.[17] Parasympathetic function was evaluated by heart rate variation during deep breathing at 6 breaths a minute for one minute and immediate heart rate response to standing (30:15 ratio). Sympathetic function was assessed by genitourinary symptoms like urinary incontinence and impotence in males, gastrointestinal symptoms like refractory diarrhoea especially at night and cardiovascular symptoms with a fall of systolic blood pressure in response to standing >20mmHg and diastolic blood pressure >10mmHg. Results of each of these tests were scored as 0=normal, 1=border line, 2=abnormal. A total of >2 score was taken as autonomic neuropathy.

Patients with cerebrovascular accident, acute myocardial infarction, cases who were on nasogastric feeding, hemodynamically unstable and those who had esophageal surgery were excluded from the study.

Table 1. Comparison of lower esophageal sphincter pressures in diabetics with and without neuropathy.

	DM with neuropathy (n=28) Mean ± S.D	DM without neuropathy (n=28) Mean ± S.D	p-value
End Inspiratory Pressure	45.62 ± 16.55	52.57 ± 21.37	0.176
Mid Expiratory Pressure	30.15 ± 11.10	34.62 ± 14.08	0.189
End Expiratory Pressure	15.30 ± 7.77	16.41 ± 8.71	0.622
Residual Pressure	1.65 ± 3.69	3.01 ± 4.16	0.201
Percent of Relaxation	91.00 ± 14.08	82.39 ± 22.70	0.090

In all statistical analysis, only p-values <0.05 are considered significant.

All the cases meeting above-mentioned criteria were recorded on a flow sheet. Their age, gender, duration of disease, height, weight, random blood sugar, HbA1C was recorded. Symptoms related to esophagus i.e. dysphagia, heartburn, regurgitation and retrosternal pain or any other symptoms were recorded.

All the steps of the procedures were explained in detail and a verbal, informed consent was taken prior to the procedure. The anxiety of the subjects was minimized by discussing and explaining the procedure to them.

Equipment and Procedure

An eight-lumen water perfused polyvinylchloride catheter, containing 8 capillary lumens of approximately 0.8mm in diameter with side openings 0.8mm in diameter around a central lumen was used. Each of the eight capillary tubes has an opening at a set point along its length. The eight orifices are numbered 1 through 8, with number 1 being the most distal and number 8 the most proximal. The four distal orifices, number 1 through 4 are 1cm apart and oriented radially at 90-degree angles. The other end of the catheter consists of eight individual capillary tubes. Each capillary tube is marked for identification and ending with a special tip for connection to the external transducers, set on a rack at the same level as the subject's esophagus in the supine position and are connected to both the hydraulic infusion pump and polygraph. The infusion pump perfuses the catheter at a constant rate and pressure.

Calibration of the transducers was done before start-

Table 2. Comparison of peristaltic amplitude and duration in diabetics with and without neuropathy.

		DM with Neuropathy (n=28) Mean ± S.D	DM without Neuropathy (n=28) Mean ± S.D	p-value
Dry Swallows (cm)				
Amplitude at	18	49.64 ± 39.20	37.04 ± 21.07	0.144
	13	41.79 ± 21.85	39.25 ± 20.39	0.659
	8	54.82 ± 33.07	50.91 ± 26.51	0.633
	3	47.09 ± 39.28	34.71 ± 33.31	0.210
	DES	50.64 ± 33.69	42.81 ± 26.22	0.336
Duration at	18	3.19 ± 0.84	3.15 ± 0.74	0.852
	13	3.65 ± 0.67	3.67 ± 0.80	0.926
	8	4.16 ± 0.92	4.10 ± 0.50	0.778
	3	4.46 ± 0.90	4.18 ± 1.16	0.667
	DED	4.35 ± 0.84	4.14 ± 0.72	0.319
Wet Swallows (cm)				
Amplitude at	18	53.83 ± 37.37	51.02 ± 28.79	0.759
	13	46.70 ± 26.32	37.56 ± 20.87	0.157
	8	72.08 ± 42.27	63.86 ± 34.80	0.430
	3	59.60 ± 38.91	43.70 ± 37.74	0.129
	DES	65.67 ± 37.28	53. 78 ± 33.13	0.212
Duration at	18	3.27 ± 1.08	3.26 ± 1.09	0.962
	13	3.76 ± 1.13	3.67 ± 1.14	0.774
	8	4.17 ± 0.19	4.04 ± 1.02	0.605
	3	4.94 ± 1.84	4.34 ± 1.55	0.204
	DED	4.57 ± 1.25	4.19 ± 1.16	0.242

In all statistical analysis, only p-values <0.05 are considered significant.

Table 3. Comparison of peristaltic velocity in diabetics with and without neuropathy.

	DM with Neuropathy (n=28) Mean ± S.D (cm/sec)	DM without Neuropathy (n=28) Mean ± S.D (cm/sec)	p-value
Dry Swallows			
Proximal Esophagus	3.05 ± 1.50	2.40 ± 1.96	0.166
Distal Esophagus	3.09 ± 1.76	3.01 ± 2.35	0.883
Wet Swallows			
Proximal Esophagus	2.08 ± 1.53	1.48 ± 3.28	0.611
Distal Esophagus	2.22 ± 1.70	2.05 ± 3.40	0.805

In all statistical analysis, only p-values <0.05 are considered significant.

Calibration of the transducers was done before starting the procedure. Patients were asked to come for the procedure after 4 hours fasting after breakfast. Detailed history was taken about any medication taken 48 hours prior to the test, to exclude any possible influence of medication (prokinetic drugs, nitrates, anticholinergics, calcium channel antagonists or sedatives) on the esophageal motility.

The catheter lumens were prefilled with sterile water and the lumens were capped to retain the fluid. The first few centimeters of the catheter was immersed in water to reduce friction during intubation and no local anaesthetic was used while passing the manometry catheter.

The subject was seated during intubation and the catheter was passed horizontally through the nares into the oro-pharynx across the upper region of the hard palate. When the catheter entered the pharynx, the subject was asked to tilt the head forward towards the chest and swallow. In difficult cases, sips of water using a straw were allowed to facilitate the entry of the catheter through the pharynx and upper esophageal sphincter.

The catheter was inserted sufficiently, so that there was no pressure measuring ports covering at least 10cm of the stomach i.e. when the 50cm mark on the tube was at the tip of the nose. Once the catheter was in position the subject was asked to lie supine with a pillow under the head and a straight head. The catheter was connected to the transducers and infusion commenced. A period of at least 10 minutes was allowed for stabilization of the subject's state and the recording system. The subject was asked to limit swallowing as the pharyngeal irritation caused by the catheter is accentuated by repeated swallowing. The catheter tips 1 through 4 were connected to the transducers and the water at the infusion pump was turned on with a transfusion rate of 0.6ml/minute.

Data analysis and functions of the upper and lower esophageal sphincters and esophageal body were assessed as described in the earlier studies.[18,19]

The computer package Microsoft Excel was used for data feeding and analysis was done by Epi-Info version 6.0. The results were given in the text as Mean and Standard Deviation (S.D.) for quantitative variables and percentages for qualitiative variables. To compare Mean and Standard Deviation for quantitative variables between groups (Diabetics and Controls, Diabetics with or without neuropathy) by student's t-test (unpaired) and compare proportion/percentages between groups by Chi-Square test. In all statistical analyses, only p-values <0.05 are considered significant.

Results

Esophageal manometric studies were done in 56 patients suffering from Diabetes Mellitus admitted in Ziauddin Hospital. There were 23 males and 33 females whose ages ranged from 28 to 80 years with a mean age of 55.2±10.2 years. Height of the patients ranged from 135cm to 178cm, with a mean height of 157.34±11.46cm. Weight ranged from 37 to 86kg, with a mean of 64±10.5kg. Duration of disease ranged from 1 to 30 years, with a mean of 9.76±6.64 years. Random blood sugar ranged from 55 to 430mg/dl, with a mean of 241.96±791.85mg/dl. HbA1C ranged from 5.4 to 19, with a mean of 8.088±2.08.

Of the 56 diabetic patients analyzed, 28 were having neuropathy, 8 of these were males and 20 were females. Of the 28 patients without neuropathy 15 were males and 13 were females. Out of 28 cases with neuropathy, peripheral neuropathy was present in all patients and autonomic neuropathy was present in 20 patients.

Comparison of data between the two groups with and without neuropathy showed that patients with neuropathy were slightly younger than those without neuropathy, mean age being 53.61±8.52 vs. 56.86±11.57 years. Gender distribution was almost equal in patients with neuropathy i.e. 15 males and 13 females, but females predominated in patients without neuropathy i.e. 8 males and 20 females. Height of the patients in the two groups was almost identical 156.54±11.8 and 158.16±11.27cms. Weight of the patients was higher in cases without neuropathy (67.06±9.63Kg) as compared to those with neuropathy (61.25±10.70Kg). BMI was also marginally higher in patients without neuropathy as compared to patients with neuropathy. Duration of the disease was longer in patients with neuropathy (12.46±6.78 years) as compared to patients without neuropathy (7.75±5.69 years).

Random blood sugar and HbA1C were higher in patients

with neuropathy (268.93±97.78mg/dl and 8.31±1.59 respectively), as compared to patients without neuropathy (215±78.19mg/dl and 7.86±2.47 respectively).

Mean End Inspiratory Pressure of the lower esophageal sphincter was higher in patients without neuropathy (52.57±21.37mmHg), as compared to patients with neuropathy (45.62±16.55mmHg). Similarly Mid Expiratory Pressure of the lower esophageal sphincter was also higher in patients without neuropathy 34.62±14.08mmHg, as compared to patients with neuropathy. End Expiratory Pressure of the lower esophageal sphincter was similar in both groups being 16.41±8.71 and 15.30±7.77mmHg respectively. Residual pressure of the lower esophageal sphincter was also higher (3.01±4.16mmHg) in patients without neuropathy, as compared to patients with neuropathy (1.65±3.69mmHg). The percentage of relaxation of the lower esophageal sphincter was higher in patients with neuropathy (91±14.08%) as compared to patients without neuropathy (82.39±22.70%) (Table 1).

Peristaltic amplitudes of the esophageal body at 18, 13, 8 and 3cms from the lower esophageal sphincter was higher in patients with neuropathy as compared to patients without neuropathy, both for dry and wet swallows (Table 2).

Duration of esophageal peristalsis at 18, 13, 8 and 3cms from the lower esophageal sphincter was almost similar in patients with and without neuropathy, and both for dry and wet swallows (Table 2).

Peristaltic velocity of the esophageal body was higher in patients with neuropathy, for both dry and wet swallows (Table 3).

Resting pressure of the upper esophageal sphincter was higher in patients without neuropathy (55.08±22.65mmHg), as compared to patients with neuropathy (47.57±17.39mmHg). Residual pressure was also higher amongst patients without neuropathy (3.57±4.09mmHg), as compared to patients with neuropathy (3.08±3.41mmHg).

Duration of relaxation (onset to neider) was marginally longer in patients with neuropathy (1.68±0.73sec), as compared to those without neuropathy (1.53±0.70). Total duration of relaxation (onset to end) was also marginally longer in patients with neuropathy (3.79±1.06sec), as compared to patients without neuropathy (3.69±0.83sec). Duration of recovery (neider to end) was longer in patients without neuropathy (2.31±0.71sec), as compared to patients with neuropathy (2.11±0.61sec). Marginal differences were noted in the duration of relaxation of the upper esophageal sphincter.

Comparison of the abnormal waves showed that double peaked waves were more common in patients with neuropathy (10 cases) as compared to those without neuropathy (2 cases). Similarly non-conducted waves were also more common in patients with neuropathy (3 cases), than those without neuropathy (1 case). High amplitude and broad peristaltic waves were more common in patients without neuropathy (4 cases) when compared to patients with neuropathy (2 cases). Achalasia was found in only one patient without neuropathy. A peristalsis of the esophageal body (4 cases) and triple peaked waves (1 case) were equally prevalent in both groups of patients.

Discussion

The present study was conducted to detect the presence of esophageal motor disorder in diabetic patients and to find out the difference between the patients with and without neuropathy. The demographic parameters of these cases i.e. age, gender, height and BMI showed no statistically significant difference in the two groups except for the heavier weight amongst patients without neuropathy.

HbA1C was higher amongst patients with neuropathy when compared to those without neuropathy but the difference could not reach statistical significance. Random blood sugar was significantly higher amongst diabetics with neuropathy as compared to those without neuropathy (p=0.025), which signifies poor diabetic control in patients with neuropathy. Poor glycemic control and symptoms has been described before[20], but no correlation has been found between the symptoms and the presence or absence of diabetic neuropathy and manometric abnormalities in this study as reported before.[21]

All parameters of lower esophageal sphincter pressures i.e. end inspiratory pressure, mid expiratory pressure and end expiratory pressure and residual pressure of the lower esophageal sphincter were higher in patients without neuropathy. The percentage of relaxation was also higher amongst patients with neuropathy but none of these differences were statistically significant. These findings are different from the earlier studies[22] which showed a decrease in the amplitude of peristalsis, a decrease in Primary peristalsis and a decrease in LES pressure in a small group of diabetics all with autonomic neuropathy. These types of findings in diabetics with[23] and without[24] neuropathy were also noted by other investigators. On the contrary no significant difference was found in the peristaltic amplitude of the esophageal body, both for dry and wet swallows, at all levels i.e. 18, 13, 8, 3cms.

The duration of peristalsis also did not show any difference in diabetics with and without neuropathy. Similarly the difference in the progression of the peristaltic waves i.e. velocity in the proximal and distal esophagus both for dry and wet swallows was not significantly different amongst

diabetics with and without neuropathy, which is contradictory to the earlier reported series in which a significant decrease in peristaltic velocity was noted in diabetics with neuropathy.[14]

In a large study examining 50 diabetics with and without peripheral neuropathy, Hollis and coworkers[12] noted a decrease in primary peristalsis (greater than 10% absence of peristaltic response to a swallow), an increase in repetitive contractions (two or more contractions in greater than 25% of swallows) and an increase in spontaneous contractions (greater than 10 during a 35-minute study), mainly in diabetics with peripheral neuropathy. There was also a significant decrease in peristaltic velocity in the diabetics with peripheral neuropathy. No differences were noted in peristaltic amplitude or LES pressure in any of the groups. More recently Loo et al.[14] have described another manometric abnormality in diabetics with peripheral neuropathy, an increased incidence of peristaltic double peaked pressure complexes. The significance of this finding remains to be determined, Since double peaked waves do occur in normal and the high incidence of double peaked waves (>95% of all peristaltic swallows) noted in their group of diabetics has not been confirmed in other diabetics studied with manometry.[25] In our study double peaked peristaltic waves were significantly higher (10 vs. 2 cases) amongst diabetics with neuropathy than those without neuropathy.

In our study non-conducting waves or failed peristalsis were more common in patients with neuropathy as compared to those without neuropathy while high amplitude and broad waves were more common in patients without neuropathy. Both of the cases with hypertensive lower esophageal sphincter were found in patients without neuropathy. Aperistalsis and multiple peaked waves were equally prevalent in patients with and without neuropathy.

Upper esophageal sphincter resting pressure, residual pressure, duration of relaxation and recovery were not significantly different in those with and without neuropathy. Later studies have also described a poor correlation between autonomic neuropathy and motor disorders.[26] Being a small group of patients studied in this series significance of all these abnormalities should be determined in a larger group of patients in further studies. Probably the use of latest technologies like 24 hour pH monitoring studies and simultaneous ambulatory impedance[27] may also help in finding differences among the two groups along with the reflux related issues.

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