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Diabetes Mellitus and Upper Gut Motility

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Abstract

The aim of the study is to detect the presence of esophageal motor disorders in type I and II diabetic patients, and to establish whether there is any difference between patients with and without neuropathy. 118 diabetic patients (34 type I and 84 type II) were investigated by water-perfused stationary esophageal manometry. Data were correlated with the presence of peripheral neuropathy. As a result 71% of patients affected by peripheral neuropathy showed manometric abnormalities against the 37% of the patients without neuropathy. Our experience has shown that patients with diabetes mellitus frequently present esophageal symptoms and manometric abnormalities. Manometric study of the esophagus has to be considered a useful investigative tool to manage and monitorize the gastrointestinal abnormalities in patients affected by diabetes mellitus.

Introduction

The diabetes mellitus (DM) is a metabolic disorder of multiple etiology characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both.
The effects of DM include long-term damage, dysfunction and failure of various organs.
The long-term effects of DM include progressive development of the specific complications of retinopathy, nephropathy that may lead to renal failure, and neuropathy both peripheral and autonomic. DM is classified in different types: type1, type2, gestational DM and less frequent as malnutrition related DM or secondary to pancreatic disease or other.
The type 1 DM constitutes the 5-10% of the total, the age of onset is usually minor than 30 and most of all minor than 20 years old. The pathophysiology is related to an auto immune mechanism in which an immune mediate reaction promoted by T-lymphocytes destroys the pancreatic B-cells with a severe and often complete insulinopenia. The causes are probably multifactorial with a genetic predisposition, an immunologic damage and surely an environmental involvement in the global damage.
Type 2 DM constitutes the 90-95% of DM diagnosis and the age of onset is generally the adult period. Signs and symptoms are usually mild or absent at time of diagnosis. It occurs due to defect in insulin function because of an insulin resistance and a decreased insulin production associated with an hepatic glucose overproduction. This multifactorial pathology is often related with obesity (80%), other metabolic pathology (MODY) and sedentary lifestyle. The genetic predisposition is also important.
The DM chronic complications are micro vascular like retinopathy, neuropathy or nephropathy, and macro vascular that involve the coronary, the cerebral and the peripheral arteries and others like the increased susceptibility to infections, the diabetic foot disorders and the cataract.
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.
Evidence for altered esophageal motor function in diabetes was first reported in 1967. Esophageal motor dysfunction has been detected by cine radiographic or manometric techniques for a long time, but so far esophageal manometry is the gold standard for the detection of esophageal motor disorders.
The sensory and motors neuropathy includes the symmetric distal neuropathy, the mono neuropathy and the amyotrophy. The symmetric distal neuropathy is most often in the lower extremities with paresthesias occurring most of all at night, the mononeuropathy affects generally the asymmetric cranial or peripheral nerves.
Most commonly these are compression neuropathy and have a spontaneous resolution in 3-6 months. The amyotrophy is generally asymmetric, is characterized by

severe pain, muscle wasting in pelvic girdle and quadriceps and usually self limiting with resolution in 6-12 months.
The autonomic neuropathy produces severe damage with visceral and cardiovascular manifestations, and a reduced perception of hypoglycemia. Visceral manifestations include gastro-esophageal paresis with nausea and vomiting, early satiety, abdominal distention and bloating; diabetic diarrhea with intermittent bouts of diarrhea and constipation and neurogenic bladder and incontinence associated to sexual dysfunction.
The decreased sensitivity associate to the micro and macro angiopathy induces also the diabetic foot disorder. More than 50% of non traumatic amputations occur in patients with diabetes.
Esophageal manometric abnormalities are common in diabetic patients with peripheral neuropathy [5-14].
The pathophysiology of these abnormalities could be related to the degenerative effects of diabetes mellitus on the autonomic nervous system, rather than smooth muscle dysfunction. However the etiology of symptoms has not been completely clarified.
Our group wanted to show the difference between manometric abnormalities in patients with and without peripheral neuropathy [15,16].

Materials and Methods

Water-perfused stationary manometry was used to assess the motor activity of the esophagus and upper (UES) and low (LES) esophageal sphincter in 118 patients, 34 type I (25 males, 9 females, average age 31) and 84 type II (38 males, 46 females, average age 71).
Autonomic neuropathy was considered by the standardized measurement of cardiovascular reflexes. 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 [17].
We couldn't register any case of autonomic neuropathy.
Esophageal manometry was performed using a water-perfused eight-channel catheter (four radial ports at the same level and four separated by 5 cm intervals) by station pull-through technique in fasting patients from at least 6 hours.
Every single channel was perfused by a capillary pneumo-hydraulic system with constant flow.
The subject was seated during intubation and the catheter was passed horizontally through the nares into the oro-pharynx.
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 10 cm of the stomach i.e. when the 50 cm 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 [18].
We analyzed basal LES position, lenght, pressure and relaxation with four radial ports. Gastroesophageal pressure gradient (GEPG) was defined as the mean difference between intragastric pressure (IGP) and LES pressure and measured using radial ports.
The primary and secondary peristaltic activity of esophageal body was assessed over 10 episodes of dry swallow and 10 episodes of wet swallow (3 cc aliquots of water).
The upper esophageal sphincter (UES) position, lenght, pressure and relaxation were evaluated using assial ports.
Every manometric test lasted about 4 hours.
The data were digitalized using a commercially available software (Flexilog 3000).
The computer package Microsoft Excel was used for data feeding and statistical analysis.
The results were given in the text as Mean and Standard Deviation (S.D.) for quantitative variables and percentages for qualitative variables. To compare Mean and Standard Deviation for quantitative variables between groups (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 performed in 118 patients suffering from DM: 34 type I and 84 type II.
In the type I group there were 25 males and 9 females whose ages ranged from 28 to 34 years (mean 31). The duration of disease ranged from 0.5 to 18 years.
In the type II group there were 38 males and 46 females whose age ranged from 62 to 80 (mean 71). The duration of disease ranged from 5 to 30 years.
Peripheral neuropathy could be register in 12 type II patients while in 106 any neuropathy sign was present.
An increase in the basic tone of the UES was observed in 18% while in 3% this was associated with its incomplete release.
In 51.6% patients we evidenced a non specific motor disturbance such as spontaneous motor activity characterised by repetitive segmentary waves at times with biphasic appearance.

In 78.6% patients a reduction in LES basic tone was observed, peculiarly associated with an asymmetry of the sphincter.
In 17 patients (71%) affected by peripheral neuropathy we could demonstrate manometric abnormalities against the 37% (39 patients) without neuropathy.

Discussion

The gastrointestinal apparatus is often involved in the DM symptomatology which involves every single part, mainly the first part of it like esophagus, stomach ad jejunum. Refers especially to the esophagus, the diabetic damage induce an important alteration of the peristaltic waves and a significative reduction of the lower esophageal sphincter (LES) pressure that become worse as time wore on and with the persistence of the hyperglycemia.
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 peripheral 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 [19].
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 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 and without 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, and 8 cms.
The duration of peristalsis showed a significative difference in diabetics with or without neuropathy. Similarly the difference in the progression of the peristaltic waves i.e. velocity in the proximal and distal esophagus especially for dry wet swallows was significantly different amongst diabetics with and without neuropathy: a significant decrease in peristaltic velocity was noted in diabetics with neuropathy, and an increased incidence of peristaltic double peaked pressure complexes [20-27].
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. All the cases with hypertensive lower esophageal sphincter (2 type I and 21 type II) were found in patients without neuropathy.
A peristaltic 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.
Probably the use of 24 hour pH monitoring studies may also help in finding differences among the two groups along with the reflux related issues.

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