ASSESSMENT OF GASTRIC NEUROPATHY USING ELECTROGASTROGRAPHY IN ASYMPTOMATIC DIABETIC PATIENTS. CORRELATION WITH CARDIAC AUTONOMIC NEUROPATHY

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SUMMARY - This study assessed gastric neuropathy in type 1 diabetes mellitus and its relationships with cardiac autonomic neuropathy. Fifty-four asymptomatic type 1 patients (43 ± 12 years) and 15 healthy subjects participated in the study. Cutaneous electrogastrography (EGG) was recorded for 4 h before, during, and 4 h after the ingestion of a standard meal. EGG frequency was divided into three bands: bradygastria (< 2 cpm), normal (2-4 cpm) and tachygastria (4-10 cpm). Assessment of diabetic autonomic neuropathy was based on Ewing tests and time and frequency domain indexes, which were analyzed from 24-h continuous ECG recordings. Tachygastria was significantly more common in diabetic patients than in controls throughout the recording period (38 ± 5 vs 23 ± 11.8%, p < 0.001), before (37 ± 6 vs 26.5 ± 8.9%, p < 0.001), during (41 ± 7.8 vs 23 ± 10.5%, p < 0.001) and after the meal (37 ± 6.9 vs 29 ± 9.8%, p < 0.001). The percentage of dominant frequency in the normal range was significantly lower in diabetic patients than controls (49 ± 6 vs 63.3 ± 11.1%, p < 0.001). Tachygastria was correlated with duration of diabetes (r = 0.234, p < 0.05), but not with glycaemic control. Abnormalities in gastric myoelectrical activity were not correlated with Ewing tests or time and frequency domain indexes.

Key-words: electrogastrography, gastric neuropathy, cardiac autonomic neuropathy, type 1 diabetes mellitus.

RÉSUMÉ - Étude de la neuropathie gastrique par électrogastrographie chez des diabétiques asymptomatiques. Corrélations avec la neuropathie autonome cardiaque.
Le but de cette étude est d’évaluer les caractéristiques de la neuropathie végétative gastrique du diabète de type 1 et ses relations avec la neuropathie autonome cardiaque. Ont été inclus dans cette étude 54 diabétiques de type 1 (moyenne d’âge : 43 ± 12 ans) asymptomatiques et 15 témoins. L’enregistrement électrogastrographique s’effectue pendant les 4 heures qui précèdent et les 4 heures qui suivent un repas standardisé. La fréquence électrique gastrique normale est comprise entre 2 et 4 cycles par minute (cpm); la bradygastrie est définie par une fréquence inférieure à 2 cpm, la tachygastrie par une fréquence comprise entre 4 et 10 cpm. L’évaluation de la neuropathie végétative cardiaque repose sur les 5 tests d’Ewing et sur l’analyse fréquentielle et temporelle du Holter ECG de 24 heures. Chez les diabétiques, la tachygastrie est plus fréquente que chez les témoins sur l’ensemble de l’enregistrement (38 ± 5 vs 23 ± 11.8%, p < 0.001), et au cours des périodes prandiales (37 ± 6 vs 26.5 ± 8.9%, p < 0.001), pendant la prandiale (41 ± 7.8 vs 23 ± 10.5%, p < 0.001) et post prandiale (37 ± 6 vs 29 ± 9.8%, p < 0.01). Par rapport aux témoins, les diabétiques présentent une réduction significative de la fréquence gastrique normale (49 ± 6 vs 63.3 ± 11.1%, p < 0.001). La tachygastrie est corrélée à l’ancienneté du diabète (r = 0.234, p < 0.05) mais pas à son équilibre. Les résultats de l’EGG ne sont ni corrélés aux résultats des tests d’Ewing ni aux données des analyses fréquentielle et temporelle du Holter ECG.

Mots-clés : électrogastrographie, neuropathie gastrique, neuropathie autonome cardiaque, diabète de type 1.
Gastrointestinal motor disorder is a frequent and well-known complication in longstanding diabetes [1]. This disorder can be assessed by gastric emptying, manometry and more recently by electrogastrography (EGG) [2], a procedure likely to prove attractive for pathophysiological study of gastric myoelectrical activity. In diabetic patients with gastroparesis, gastric dysrhythmias are generally considered to be involved in the pathogenesis of dyspeptic symptoms, although some studies have recorded them even in asymptomatic patients [3] and correlations between EGG parameters and gastrointestinal symptoms have not always been found [4]. Diabetic autonomic neuropathy could account for this lack of correlation as it does for the lack of ischaemic pain in diabetic patients with coronary artery disease. This study investigated the characteristics of gastric motility disorder in asymptomatic diabetic patients by EGG and evaluated the correlation between these abnormalities and cardiac autonomic neuropathy.

## SUBJECTS AND METHODS

**Patients** – Fifty-four insulin-dependent diabetes mellitus patients (mean age 43 years, range 22-70) and 15 healthy age- and sex-matched non-diabetic subjects were studied (see Table I for clinical characteristics). Diabetic patients were asymptomatic, with no complications, and none were receiving medical treatment except insulin.

**Assessment of gastric neuropathy** – Electrogastrography (Digitracker EGG, Synthsics Medical) was performed by placing three surface electrodes on epigastric skin. The EGG signal was recorded for 4 h before, during and 4 h after ingestion of a 760 kcal standardised meal containing 102 g of carbohydrate, 23 g of fat and 38 g of protein. All meals (100 g of salad, 150 g of chicken or rabbit or turkey, 250 g of rice or noodles, 10 g of butter, 1 yoghurt, 1 fruit and 60 g of bread) were consumed within 30 min. The dominant frequency and power of EGG were determined using running spectral analysis, and the time-course was evaluated on a three-dimensional graph. The EGG variables studied were the percent of electrical dysrhythmias [bradygastria: 0.5-2 cycles per min cpm; tachygastria: 4-10 cpm (normal rhythm 2-4 cpm)]. These percentages were compared for diabetic and control subjects over the entire recording period and during the fasting state, the period of meal consumption and for 4 h after ingestion of the test meal. Running spectral analysis is shown in a control subject (Fig. 1) and a diabetic patient with tachygastria (Fig. 2).

**Assessment of cardiac autonomic neuropathy** – Autonomic nerve function was assessed using Ewing cardiovascular reflex tests performed and evaluated in accordance with the procedure described by Ewing et al. [5]. Parasympathetic function was assessed by heart rate variation to deep breathing.

| Table I. Clinical characteristics of diabetic patients and healthy control subjects. |
|-----------------|-----------------|-----------------|-----------------|
|                 | Diabetic subjects (n = 56) | Healthy controls (n = 15) | p value |
| gender (M/F)    | 13/51            | 3/12            | NS             |
| age (years)     | 43 ± 12          | 36 ± 19         | NS             |
| duration of diabetes (years) | 13,8 ± 10,4 | ND               |
| HbA1c           | 8,3 ± 1,7        | ND               |
(inspiration/expiration difference): normal ≥ 15, borderline 11-
14, abnormal < 10; heart rate response to standing up
(30/15 ratio): normal ≥ 1.04, borderline 1.01-1.03, abnormal < 1;
and Valsalva’s manoeuvre with calculation of the ratio of the
longest RR interval after the manoeuvre to the shortest RR inter-
val during the manoeuvre: normal ≥ 1.21, borderline 1.11-1.20,
abnormal < 1.1. Sympathetic function was evaluated by regis-
tering the blood pressure response to standing up: normal < 10 mmHg, borderline 11-29, abnormal ≥ 30 mmHg, and the sustained handgrip (maximum-minimum diastolic blood
pressure): normal > 16 mmHg, borderline 11-15, abnormal ≤ 10 mmHg. The results were scored as 0: normal, 0.5: border-
line, 1: abnormal. The presence of cardiac autonomic neuropathy
was defined by a total Ewing score above 2. Ambulatory 24-h
electrocardiogram monitoring (ECG Holter Elatec, HRV
Software, Ela Medical, France) was performed in diabetic pa-
tients. This programme produces the following time domain
indexes: SD of all 24-h R-R intervals (intervals between con-
secutive electrocardiogram R waves or SDNN/24-h), pNN50 (per-
centage of R-R intervals differing by more than 50 ms) and
rMSSD (root-mean-square of the differences of successive R-R
intervals). The first index expresses total HRV and the last two
reflect vagal tone. Power spectrum analysis of RR interval varia-

TABLE II. Percentages of bradygastria (0.5-2 cpm), normal range (2-
4 cpm) and tachygastria (4-10 cpm) in the entire period of recording.

<table>
<thead>
<tr>
<th></th>
<th>IDDM patients</th>
<th>Controls</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5-2 cpm</td>
<td>8,9 ± 1,9</td>
<td>8 ± 1,6</td>
<td>NS</td>
</tr>
<tr>
<td>2-4 cpm</td>
<td>49,2 ± 6,1</td>
<td>63,3 ± 11,1</td>
<td>&lt; 0,01</td>
</tr>
<tr>
<td>4-10 cpm</td>
<td>38 ± 4,9</td>
<td>23,1 ± 11,7</td>
<td>&lt; 0,01</td>
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</tbody>
</table>

TABLE III. Percentages of dominant frequency in normal range (2-
4 cpm) in the entire period of recording and in pre, per and post prandial periods in diabetic patients and in control subjects.

<table>
<thead>
<tr>
<th></th>
<th>IDDM patients</th>
<th>Controls</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire period</td>
<td>49,2 ± 6,1</td>
<td>63,2 ± 11,1</td>
<td>&lt; 0,01</td>
</tr>
<tr>
<td>Preprandial</td>
<td>49,1 ± 7,4</td>
<td>60,4 ± 9,6</td>
<td>&lt; 0,01</td>
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<tr>
<td>Perprandial</td>
<td>46,8 ± 9,4</td>
<td>65,7 ± 12,2</td>
<td>&lt; 0,01</td>
</tr>
<tr>
<td>Postprandial</td>
<td>50,8 ± 8,5</td>
<td>61,1 ± 10,9</td>
<td>&lt; 0,01</td>
</tr>
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</table>

TABLE IV. Percentages of tachygastria (4-10 cpm) in the entire pe-
riod of recording and in pre, per and post prandial periods in diabetic
patients and in control subjects.

<table>
<thead>
<tr>
<th></th>
<th>IDDM patients</th>
<th>Controls</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire period</td>
<td>38 ± 4,9</td>
<td>23,1 ± 11,7</td>
<td>&lt; 0,01</td>
</tr>
<tr>
<td>Preprandial</td>
<td>37 ± 6</td>
<td>26,5 ± 8,9</td>
<td>&lt; 0,01</td>
</tr>
<tr>
<td>Perprandial</td>
<td>41 ± 7,8</td>
<td>23 ± 10,5</td>
<td>&lt; 0,01</td>
</tr>
<tr>
<td>Postprandial</td>
<td>37 ± 6,9</td>
<td>29 ± 9,8</td>
<td>&lt; 0,01</td>
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</table>

§ RESULTS

Throughout the recording period, diabetic patients
showed a significantly lower percentage of normal slow waves than did controls. The percentage of bra-
dygastria did not differ significantly between the two
groups, and tachygastria was significantly more com-
mon in diabetic patients (Table II). During the fasting
state and the period of meal consumption, as well as
during the postprandial period, the percentage of do-
mainant electrical frequency (ratio between the power at 2-4 and 1-10 cpm) was significantly lower in diabe-
tic patients (Table III). The percentage of tachygastria
was higher in diabetic patients than in controls during
the same periods (Table IV).

No significant correlation was found between pa-
tient age and EGG results, nor between the levels of

HbA1c and EGG dominant frequency. Duration of diabe-
tes was significantly correlated with the degree of tachygastria (r = 0.349, p < 0.05). Ewing cardiovas-
cular tests and 24-h taping results are shown in Ta-
ble V. There was no correlation between the Ewing
score and EGG results. Analysis of EGG and 24-h
ECG recordings showed that HRV time and frequency
domain indexes were not correlated with gastric
myoelectrical activity: no correlation between day or night period power of low- and high-frequency components was found. When time domain indexes were studied, no correlation was found between pNN 50, SDNN/24-h and rMSSD and EGG dominant frequency.

## DISCUSSION

Gastrointestinal motor complications can be detected in up to two-thirds of patients with diabetes [1, 6]. In the present study conducted in asymptomatic patients, these gastrointestinal motor complications were characterised by an increase in the percentages of frequency in the tachygastria range. Similar abnormalities were noted in a previous study [7], but increased EGG frequencies have not been found by all investigators. The conclusions of another study in 18 insulin-treated Type 2 diabetic patients with chronic dyspepsia found that EGG results did not differ significantly between diabetic patients and control subjects [8]. In the study of Jebbink et al. [4], 30 patients with Type 1 diabetes mellitus and 12 control subjects had no disturbances in myoelectrical activity except when they were symptomatic (4). In asymptomatic insulin-dependent diabetes mellitus, Mantides et al. [3] found an increased presence of bradygastria throughout the recording period and during the fasting state as well as during the period of meal consumption. Moreover, Mintchev and Bowes [9], when comparing tachygastrias in internal and cutaneous recordings, showed that it was possible to record EGG tachygastria signals even when they were not present on the internal recording. These differences in results could have been due to the lack of standardisation of the EGG recording, especially for the duration of the fasting state, meal consumption and the postprandial period. Recently, Lindberg et al. [10] evaluated a new system for 24-hour ambulatory electrogastrography (10), which still requires technical improvements but shows a circadian variation in frequency not taken into account with short recordings. Electrogastrography dominant frequency is divided into three bands (bradygastria, normal and tachygastria), but the definition of these bands often varies in studies. The qualitative and quantitative aspects of the meal, which could act on EGG results, are not standardised.

Among investigational procedures, gastric emptying scintigraphy is the reference test for assessing the effects of gastrointestinal tract motor abnormalities [11]. However, few studies have compared results obtained with scintigraphy and EGG, and the findings are often contradictory. In patients with functional dyspepsia, Pfaffenbach et al. [12] found a close correlation between EGG data and the results of gastric emptying scintigraphy. Dyspeptic symptoms were not correlated with radioscintigraphy and EGG data, but patients exhibiting impaired gastric emptying had more tachygastrias than those with normal gastric emptying. In another study conducted in diabetic patients, Pfaffenbach et al. [8] showed the lack of correlation between EGG values, which did not differ significantly from those in control subjects, and scintigraphic results. Parkman et al. [13] found that EGG abnormalities were more often observed in patients with dyspeptic symptoms and delayed gastric emptying and suggested that EGG and gastric scintigraphy are complementary in the assessment of dyspepsia. EGG abnormalities, i.e. tachygastrias, could account for delayed gastric emptying. When studying the effect of long-term cisapride, Rothstein et al. [14] showed that dysrhythmias were one of the aetiologies of gastroparesis and that a normalisation of EGG data was associated with a greater gastric emptying rate.

<table>
<thead>
<tr>
<th>Ewing tests</th>
<th>24 hours</th>
<th>Day time</th>
<th>Night time</th>
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</thead>
<tbody>
<tr>
<td>Total power (TP, ms²)</td>
<td>3253 ± 2287</td>
<td>2935 ± 5041</td>
<td>4009 ± 3047</td>
</tr>
<tr>
<td>Lower frequency power LFP (% TP)</td>
<td>25,84 ± 7,49</td>
<td>26,78 ± 8,7</td>
<td>24,98 ± 8,19</td>
</tr>
<tr>
<td>High frequency power HFP (% TP)</td>
<td>7,39 ± 4,18</td>
<td>6,36 ± 2,93</td>
<td>8,81 ± 6,37</td>
</tr>
<tr>
<td>SDNN (ms)</td>
<td>56,8 ± 21</td>
<td>53,68 ± 20,09</td>
<td>59,74 ± 25,04</td>
</tr>
<tr>
<td>pNN50 (%)</td>
<td>9,25 ± 9,7</td>
<td>6,71 ± 7,51</td>
<td>14,13 ± 15,9</td>
</tr>
<tr>
<td>rMSSSD (ms)</td>
<td>32,1 ± 16,5</td>
<td>27,61 ± 12,76</td>
<td>38,22 ± 24,36</td>
</tr>
</tbody>
</table>
In diabetic patients with gastroparesis histological examination revealed no morphologic abnormalities of the vagal nerve [15], although disorders in gastric motility are thought to occur as a result of autonomic neuropathy [16]. Tachygastria could be due to vagal nerve damage, which is not irreversible. Some parameters, such as the percentages of dominant frequency in the normal range, improved after glycaemic control (17). Hyperglycaemia should be an important factor in the development of gastric disturbances, as it is in all diabetic degenerative complications. In Type 1 diabetic patients, hyperglycaemia is often associated with tachygastria, and when euglycaemia is obtained, EGG data do not differ significantly between diabetic patients and control subjects [18]. Vagal dysfunction, which is closely linked to glycaemic control, could be dependent on many other factors such as duration of diabetes, which was correlated with tachygastria degree in the present study.

No significant correlation was found between the five standard cardiovascular tests of autonomic function and the EGG dominant frequency. The total sum of the three parasympathetic tests was not correlated with the degree of tachygastria. Time domain indexes and frequency domain indexes, which reflect vagal tone (pNN50 and rMSSD, HFP), were not correlated with EGG parameters. According to these data, there was no link between cardiac autonomic neuropathy parameters and gastric dysmotility. In the study of Jebbink et al. [4], no correlation was found between EGG results and the severity of cardiac autonomic neuropathy. In insulin- or non-insulin-dependent diabetes mellitus with autonomic neuropathy, Kawagishi et al. [17] found a significant lower percentage of dominant electrical frequency in the normal range than in either diabetic patients without autonomic neuropathy or control subjects. According to other studies conducted under euglycaemic conditions, gastrointestinal dysrhythmias are not correlated with the presence of cardiac autonomic neuropathy [19].

CONCLUSION

Our study shows that EGG could be a relevant technique for the detection of gastric dysrhythmias present in diabetic patients without gastrointestinal symptoms. As disorders of gastric motility and gastric emptying can disturb glycaemic control, EGG could be performed to detect these disorders in patients with poor glycaemic control.

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