Electrogastrographic Findings in Cerebral Palsy Patients

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Abstract: Objectives: This work was designed to detect any changes in the gastric electrical activity and gastrin levels in infants with cerebral palsy (CP) and correlate them to the clinical findings.
Patients and methods: The study was conducted on 30 CP patients in comparison to 12 age and sex matched clinically healthy infants. All enrolled infants and children were initially subjected to complete history taking with special emphasis on gastrointestinal symptoms, clinical examination and routine laboratory procedures as well as total serum gastrin hormone by ELISA. Electrogastrographic (EEG) recording for gastric electrical activity was performed for all subjects upon enrollment.
Results: The initial power ratio was non-significantly higher in CP patients compared to the controls while the dominant frequency (DF) was non-significantly lower. Regarding the initial visual analysis of the EGG, ١٣ patients (٤٣.٣%) were normogastric compared to bradygastria in 16 (٥٣.٣%) of them. Initial serum gastrin was higher in CP patients compared to the controls. The regression analysis revealed that gastrin was the most determinant factor for dominant frequency values followed by the power ratio in the CP patients.
Conclusion: In conclusion, CP patients have disturbed gastric motility which explains the different proximal gastrointestinal clinical manifestations experienced by our patients and this should be considered during their nutritional rehabilitation programs.

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1. Introduction:

Cerebral palsy (CP) refers to a group of childhood neurologic syndromes (pyramidal and extrapyramidal subtypes) resulting from a wide variety of genetic and acquired insults to the developing brain, with abnormalities in tone, posture, and movement on clinical examination [1, 2].

The survival of children with severe central nervous system damage has created a major challenge for medical care [1, 3]. Numerous clinical reports, in small series of patients, have indicated that brain damage may result in gastrointestinal (GI) dysfunction [4, 5].

A number of investigators have reported that neurologically handicapped children have abnormalities of lower esophageal function [6] and delayed gastric emptying is common in such patients [7]. Additionally, foregut dysmotility was previously reported in children with cerebral palsy [5, 7].

Gastrointestinal motility is defined as the action enabling the passage of food and waste products through the four main regions of the digestive system: esophagus, stomach, small intestine, and large intestine or colon. Gastric motility is regulated by a variety of mechanisms to insure that it occurs at a rate optimal for the digestion and absorption of nutrients and neutralization of gastric contents as neural and hormonal mechanisms [8]. Gastric motility can be evaluated by many methods as gastric emptying time, Electrogastrography, antroduodenal manometry, barostat studies and other newer methods for evaluation.

Gastrin is a gut hormone produced by cells called G cells in the lateral walls of the glands in the antral portion of the gastric mucosa. In addition, it is also found in the anterior and intermediate lobes of the pituitary gland, in the hypothalamus and medulla oblongata, and in the vagus and sciatic nerves. Stimulation of gastric motility is probably a physiologic action. Gastrin causes contraction of the musculature that closes the gastro esophageal junction [9]. It may have a physiological role in regulating proximal gastric mechanics by inducing gastric fundal relaxation and increasing gastric wall compliance. The effect of gastrin is dependent on acid secretion [10].

Hence, the aim of this study was to detect any changes in gastric electrical activity and serum gastrin hormone levels in CP patients and correlate them to the clinical findings.

2. Patients and methods:

This study was a cross- sectional, case-control study conducted on 30 children with CP following up in the Out-patient Pediatric Neurology Clinic, Ain-Shams University, in the period from March 2007 to September 2007.

The CP patients were 17 males and 13 females, with mean age of 6.38±3.77 years. They were compared to 12 clinically healthy children serving as a control group who were 6 males and 6 females with mean age of 7.50±2.24 years. The study was conducted after obtaining an approval from the Pediatric board at the children`s Hospital, Ain Shams University and taking an informed consent from the subjects' parents or caregivers.

Enrolled patients were free of any infection, with no history of epilepsy, or any other chronic disease or drug that might affect gastric motility and secretion.

All patients and controls were subjected to detailed history taking including perinatal, developmental and dietetic history as well as symptoms of GIT disturbance and feeding problems. Thorough clinical examination was done laying stress on anthropometric measurements and full neurological examination with special emphasis on the motor system.

Weight was measured using regularly calibrated scale with minimal clothing. Height was measured using a special board calibrated in centimeters and millimeters. Weight and height, were plotted against the percentiles to obtain the percent from the median for age. Body mass index (BMI): [Wt (kg)/ Ht2 (m)] was calculated from the previous weight and height measurements.

Routine laboratory procedures were performed including complete blood count, total protein and serum albumin as well as total serum gastrin hormone by ELISA using the Kit supplied by BIOHIT plc. (Biohitplc. Laippatie 1 Fin-0088 Helsinki, Finland). Normal fasting gastrin levels in our studied age group was considered as follows; 3-4 hours: 0.96-80.8 pmol/L, 5-6 hours: 1.44-56.3 pmol/ L, >8 hours: 0.48-60pmol/L [11].

Venous blood samples were collected under complete aseptic conditions from all enrolled subjects while fasting. The samples were divided into two halves the first was taken on EDTA for the complete blood count and the remaining part was kept in a dry sterile tube from which serum was separated by centrifugation. Samples for gastrin hormone were stored at -70^{o} C freezers till the time of test procedures.

Electrogastrographic recording for gastric electrical activity was done for all subjects upon enrollment. Recording was done from five disposable pre gelled silver/silver chloride surface electrodes placed on the upper abdomen after the skin had been carefully abraded to decrease resistance to obtain a good signal to noise ratio [12]. Infants and children under examination were kept in a reclining position to minimize motion artifact. Four electrogastrography (EGG) signals were recorded bipolarly from these five electrodes as the potential differences between each of the four electrodes. A reference electrode was placed at the left clavicle. The electrical signal was recorded with appropriate amplification and filtering. Filtering is needed to exclude cardiac and small intestinal electrical activity artifacts as well as respiratory and movement artifacts [13].

One hour recording was done while the patients were fasting then they were given a standardized test meal. The test meal was a semisolid one (milk, rice and high protein additive) which was adjusted to provide a volume of 20 cm^3/kg/feed and a caloric value of one eighth of the daily needs that are approximately 100 kcal/kg/day then post prandial recording was done for one hour [14].

EGG recordings were analyzed by computer using the Fast Fourier Transform (FFT) to detect the dominant frequencies in fasting and post prandial time periods. The FFT transforms the signal from the time domain to the frequency domain. An extension of the FFT technique is the so called Running Spectrum Analysis (RSA). In this technique power spectra of short over lapping stretches of EGG signals are computed and displayed as a function of time [15].

The following parameters were evaluated for each patient:

1. Mean dominant frequency (DF): The frequency of gastric peak was determined by the absolute peak value, and the mean frequency was computed by averaging the individual spectra.
2. Power ratio (PR): The ratio of power of the mean spectrum of post prandial state to the power of the mean spectrum of the fasting state. It is indicative of the post prandial increase in gastric motor activity and was calculated for the total post prandial period [16].

Higher harmonics were identified in the spectrum using the criteria that occur at frequencies that are exact multiples of the fundamental frequency and their power should be at least 5% of the power of the fundamental component. The early post prandial frequency dip of the normal 3 cycles per minute (cpm) gastric component was identified. A rhythmic electrical activity ranging from 2.5-3.75 cpm was defined as normal gastric electrical activity. Tachygastria was considered to be present when the power spectrum contained a sharp peak component with a frequency more than 3.75 cpm and less than

10.8 cpm. For a definite diagnosis of tachygastria it was required that at the same time the normal gastric signal was absent in all four EGG signals and that the abnormal rhythm was present for at least 2 min. When a tachygastric frequency was found in the presence of a normal gastric signal the diagnosis of tachygastria was considered probable but not definite.

Bradygastria was considered to be present when the dominant peak was less than 2.5 cpm. A dysrhythmic episode had to be present at least for 2 minutes with the absence of normal gastric signal [17].

The standard computer program SPSS for Windows, release 10.0 (SPSS Inc, USA) was used for data entry and analysis. All numeric variables were expressed as mean ± standard deviation (SD) as well as median [interquartile range (IQR)]. Kalmogrov Smirnov test was used to differentiate parametric from non parametric data. Comparison of different variables in various groups was done using student t test and Mann Whitney test for normal and nonparametric variables respectively. Chi-square (χ^2) test was used to compare frequency of qualitative variables among the different groups. Spearman's correlation test was used for correlating non-parametric variables. For all tests a probability (p) less than 0.05 was considered significant. Graphic presentation of the results was also done [18].

3. Results:

The results of the current study revealed that CP patients and the controls had matching age and sex. Repeated vomiting was present in 46.7% of our CP patients, 50% had chronic constipation and 36.7% suffered from gaseous distension. The CP patients were all non ambulatory and had significantly lower weight %, BMI as well as weight for age z scores compared to the controls (table 1). Additionally, although CP patients had lower hemoglobin levels and higher white cell counts, these comparisons were of no statistical significance.

As regard the EGG study, table (2) shows that CP patients had non-significantly higher PR and non-significantly lower DF compared to the controls. Additionally, table (3) demonstrated that by visual analysis more CP patients had bradygastria compared to the controls yet this result didn't reach statistical significance.

There was a highly significant lower DF in patients who complained of vomiting compared to those who didn't [mean values are 1.35±0.78 and 2.83±0.68 respectively and z (p) is 3.40 (<0.001)], while their mean PR was higher yet the latter comparison didn't reach statistical significance [mean values are 2.60±1.80 and 1.82±0.95 respectively and z (p) is 0.42 (>0.05)]. Additionally, 14 of the 15 children who suffered from vomiting had dysrhythmia.

Similarly, there was a highly significant lower DF in patients who complained of constipation compared to those who didn't [mean values are 1.33±0.63 and 2.95±0.66 respectively and z (p) is 4.16 (<0.001)], while their mean PR was higher yet the latter comparison didn't reach statistical significance [mean values are 2.57±1.85 and 1.84±0.97 respectively and z (p) is 0.33 (>0.05)].

Regarding serum gastrin, Fig (1) shows that the CP patients had significantly higher levels compared to the controls yet both patients and controls had their gastrin values within normal levels for age and sex.

Significant negative correlation was detected between serum gastrin levels and weight percentage for age (r = -0.495 and p<0.05) (Fig 2). Meanwhile there were no statistically significant correlations between DF and PR and weight percentage for age. There were no statistically significant correlations between serum gastrin, dominant frequency or power ratio and BMI.

Studying the effect of various studied parameters on dominant frequency of EEG in patients using multiple regression test revealed a significant effect (f = 2.50, p=0.06). Further analysis revealed that the factors causing this significance are serum gastrin (beta coefficient = -0.42 and p=0.03) and power ratio (beta coefficient = -0.42 and p=0.03) in the presence of the other studied factors.

Table (1): Comparison between the anthropometric measurements of the patients and controls.

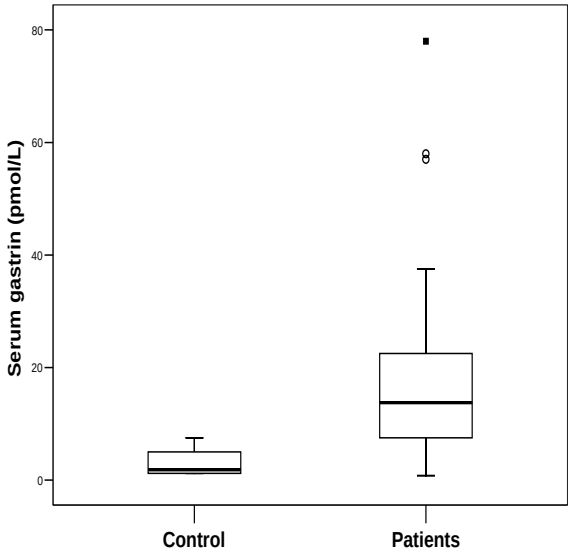
Variable	Patients		Controls		t/z*	p
	Mean±SD	Median(IQR)	Mean±SD	Median(IQR)		
Weight percentage from median for age	69.58±16.53	71.50 (22.00)	92.67±6.87	90.00 (9.00)	6.39	<0.001
Body mass index	15.13±3.82	14.05 (3.83)	20.27±5.58	18.45 (7.00)	-3.45*	<0.05
Height percentage from median for age	85.93±7.74	87.00 (12.00)	90.33±3.55	90.50 (7.00)	-1.87*	>0.05
Weight for age Z score	-2.58±1.37	-2.50 (2.10)	-0.53±0.55	-0.64 (0.81)	4.99	<0.001

Table (2): Comparison between patients and controls regarding power ratio and dominant frequency of the EGG study.

variable	Patients		Controls		z	p
	Mean±SD	Median(IQR)	Mean±SD	Median(IQR)		
Power ratio	2.21±1.50	1.49 (2.50)	1.53±0.60	1.60 (1.10)	-1.00	>0.05
Dominant frequency (cpm)	2.14±1.04	2.32 (2.20)	2.41±1.18	3.09 (2.40)	-0.84	>0.05

Table (3): Comparison between patients and controls regarding visual analysis of the EGG study

Variable		Patients number (%)	Controls number (%)	χ^2	p
Visual analysis	Normogastric	13.00 (43.30%)	8.00 (66.70)	2.05	>0.05
	Bradygastric	16.00 (53.30%)	4.00 (33.30)		
	Tachygastic	1.00 (3.30%)	0.00 (0.00)		



P=0.01

Figure (1): Serum Gastrin of patients and control groups.

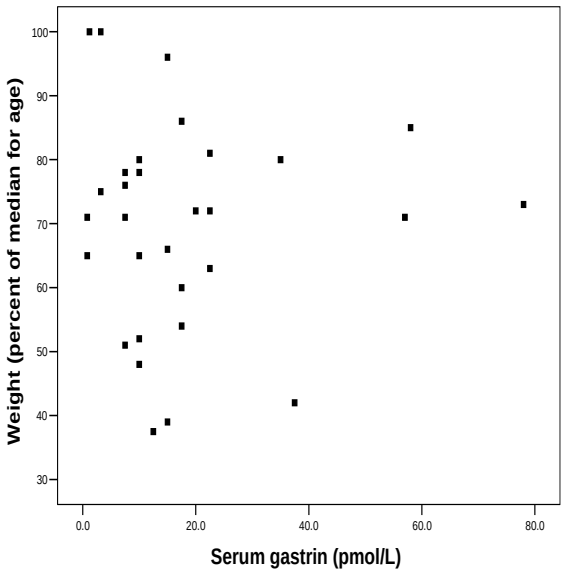


Figure (2): Serum gastrin levels with weight percentage for age of patients.

4. Discussion:

The current study revealed that the weight %, the body mass index and the weight for age Z score were statistically lower in CP patients when compared to those of the controls. Additionally, 76% of our series of CP patients had failure to thrive (mean BMI <19 [19] and Z score ≤-2 [20]).

In agreement with our results, Hurvitz et al., [21] who investigated the prevalence of overweight in a clinic-based population of children with CP and its association with gross motor function status reported that analysis of BMI in their study suggested that ambulatory children with CP had a high rate of overweight and are at risk of overweight than normal controls. On the other hand, they found that underweight is more prevelant in non ambulatory children, which is the case in our series of patients. Additionally, Feeley et al., [22] concluded that in an ambulatory CP population, patients with lower functional status or quadriplegia had significantly lower body mass index, suggesting that even highly functioning ambulatory CP patients are at risk for malnutrition.

Moreover, both Del Giudice et al., [5] who studied gastrointestinal manifestations in children with CP and Reyes et al., [23] who studied gastro esophageal reflux in children with CP, found that 52% of patients suffered from failure to thrive. Moreover, Ravelli and Milla [7] who studied vomiting and gastroesophageal motor activity in children with disorders of the central nervous system (CNS) reported that 62% of patients showed failure to thrive.

In an attempt to find the causes behind this problem, Vik et al., [24] suggested that this may in part be due to the cerebral injury and central dysfunction, in addition to the insufficient nutrition and lack of ability to self-feed.

As regards chronic GIT problems, 46.7% of our patients suffered from chronic vomiting, 50% had chronic constipation and 36.7% suffered from gaseous distension. In agreement with these findings, Ravelli and Milla, [7] found that all patients in their study suffered from vomiting and 46% of patients suffered from constipation. They concluded that in patients with CNS disorders, at least, the extrinsic innervation is abnormal, with gastric antral dysrhythmia resulting from abnormal activation of the efferent limb of the emetic reflex or from lack of inhibition of excitatory fibers as a consequence of either disturbed input to the hindbrain from higher centers or anatomic and functional disturbances of the vomiting centre and the area postrema. They demonstrated that most children who have brain damage have gastrointestinal impairments and that vomiting is a severe manifestation with significant morbidity which may persist even after surgery.

Similarly, Werlin [25] studied antroduodenal motility in neurologicaly handicapped children with feeding intolerance and found that 50% of patients suffer from vomiting. The author concluded that symptoms present in these patients might be due to an underlying forgut motor disorder.

Moreover, Del Giudice et al., [5] found that 91% of patients affected by CP had gastrointestinal symptoms. They also demonstrated that gastrointestinal motor dysfunctions are known to occur frequently in children with different degrees of brain damage and in neurologically impaired children and that the degree of GI dismotility seems to correlate with the degree of CNS damage. They confirmed that in this subset of children, chronic constipation is mainly due to prolonged transit at level of the more proximal segments of the colon. The authors further added that no child with CP presented with chronic constipation associated with soiling in contrast with neurologically normal children in whom constipation is characterized by fecal soiling.

In the current study, we found that, there was no statistical significant difference in gastric motility, as denoted by the power ratio and the dominant frequency of the EGG study, between patients and controls. However, the median values of the power ratio and the dominant frequency of the patients were lower than those of the control group. Additionally, there were no statistical significant differences between patients and controls as regard the qualitative visual analysis of the EGG study, yet the percentage of individuals with gastric motility dysfunction was more in patients (53.3% bradygastric, 3.3% tachygastric) than controls (33.3% bradygastric, 0% tachygastric).

Similarly, Ravelli and Milla [7] found that 62% (31/50) of patients with CNS disorders had antral dysrhythmia. Four had bradyarrhythmia, 12 had tachyarrhythmia, 12 had unstable electrical activity and 3 had mixed dysrhythmia in which no dominant frequency could be detected. They concluded that antral dysrhythmias could be caused by disordered intrinsic nerves of the enteric nervous system. Since their patients had various types of gastric antral dysrhythmias characterized by slower, faster, or disorganized electrical activity, they explained that this variability may be the consequence of the variable etiology, pathology, severity and site of neural lesions at the level of the CNS or the enteric nervous system.

Additionally, Werlin [25] studied antroduodenal motility in neurologically handicapped children with feeding intolerance and found that all

studied children had abnormal antroduodenal motility. The author concluded that in neurologicaly handicapped children, foregut dysmotility may be more common than is generally recognized and can explain many of the upper gastrointestinal symptoms in neurologically handicapped children.

In the current study, we found that there was a highly significant lower dominant frequency in patients who complained of vomiting compared to those who didn't; while their mean of power ratio was higher yet the latter comparison didn't reach statistical significance. Additionally, 14 of the 15 children who suffered from vomiting had dysrhythmia.

In agreement with our results, Ravelli and Milla, [7] found that 62% of children with disorders of the CNS and vomiting had antral dysrhythmia while patients without vomiting had similar dominant frequency as that of controls. They concluded that vomiting is related to gastric dysrhythmias and delayed gastric emptying possibly due to activation of the emetic reflex at least as often as gastroesophageal reflux.

Similarly, Miki et al., [26] in a study about antroduodenal motor function and gastro-oesophageal reflux in neurologically impaired children, reported that fasting antroduodenal motility was abnormal in 11 neurologically impaired children with vomiting. In 1998, Levanon and Chen [27] reported that impaired myoelectrical activity observed in the EGG is associated with disturbed motility and upper gastrointestinal symptoms (nausea, vomiting, abdominal pain) and suggested that EGG could be a useful tool in the primary evaluation of symptoms suggestive of gastroparesis.

In the current study, we found that there was highly significant lower DF in patients who had constipation compared to patients with no constipation. In agreement with our results, Ravelli and Milla [7] found that 60% of patients with disorders of the CNS and gastric dysrhythmia suffered from constipation. They concluded that chronic constipation might affect the motor activity of the stomach and the proximal small bowel.

In the current study both the patients and the control groups showed within normal fasting gastrin levels for age. Nevertheless, statistically significant higher fasting gastrin levels were found in CP patients. Meanwhile, no statistical significant difference was detected between hypertonic and hypotonic CP patients as well as those with GIT complaints versus those without.

Although many studies reported the gastrin increases gastric motility [28], yet relatively higher gastrin levels were associated with the predominance of bradygastria in our series of patients. We hypothesize that these results could be attributed to the fore-mentioned malnourished state of our CP patients which could have consequently lead to gastric mucosal atrophy [29] and/or gastric acid hyposecretion that in turn increases gastrin as a feedback mechanism [30–32]. In support of this point is the statistically significant negative correlation between serum gastrin levels and the weight percent detected in our series of patients.

Additionally, it was reported that gastrin strengthens the antral contractions against the pylorus, and constricts the pyloric sphincter, which has the effect of slowing the rate of gastric emptying [33]. Meanwhile other authors had concluded that injection of gastrin delays gastric emptying either directly [34-36] or through gastric acid action [10, 37]. The high gastrin found could thus be considered among the causes of the detected gastric motility disturbances in our series of patients. The previous point is further reinforced by the regression analysis of data which revealed that gastrin was the most determinant factor for dominant frequency values followed by the power ratio in our series of CP patients.

In conclusion, CP patients have disturbed gastric motility which explains the different proximal gastrointestinal clinical manifestations experienced by our patients and the disturbed gastrin levels could be considered among the causes. We thus recommend further larger scale studies to study the other hormonal and non hormonal factors affecting motility in CP patients; meanwhile, their feeding protocols should include small frequent meals in a semisolid rather than solid nature to overcome the gastric dysrrhythmias and delayed gastric emptying that they could subsequently suffer from.

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