Electrogastrography in children with cerebral palsy: Abnormal postprandial response to both fast- and slow-emptying meals

Anne C. Brun a, *, Edda J. Olafsdottir b, Beint S. Bentsen a, Ketil Stordal c, d, Groa B. Johannesdottir e, Asle W. Medhus a

a Oslo University Hospital, Ullevål, Norway
b Haukeland University Hospital, Bergen Hospital Trust, Norway
c Østfold Hospital Trust, Fredrikstad, Norway
d Norwegian Institute of Public Health, Norway
e Akureyri Hospital, Iceland

1. Introduction

Recurrent vomiting is a major problem for children with disorders of the central nervous system (CNS). Several mechanisms are involved and gastric antral dysrhythmias and delayed gastric emptying (GE) are at least as common as acid gastro-oesophageal reflux disease (GORD) [1]. These patients are often in need of a gastrostomy, and following gastrostomy tube placement, some children develop gagging, retching, more vomiting, pain or irritability during feeding [2]. This may reflect an underlying gastric motility disorder [3].

Electrogastrography (EGG) is a method for recording gastric myoelectrical activity using cutaneous electrodes placed on the anterior abdominal wall overlying the stomach. EGG measures slow waves (SW), rhythmic electrical depolarizations, and the gastric SW...
determine the maximum frequency and propagation of gastric contractions. The interstitial cells of Cajal generate the rhythmic depolarizations of the gastric SW occurring at a frequency of 3 cycles per minute (cpm) in humans [4]. Frequencies of the SW outside its normal rate of 2–4 cpm are classified as dysrhythmia, or bradygastria (<2), tachygastria (>4) or arrhythmia (no identifiable predominant frequency). However, the validity of the terms bradygastria and tachygastria as diagnoses has been questioned as there is no consensus concerning percentage of time spent in the bradygastric and tachygastric range required to be classified as pathological [5]. The recorded signal is called the electrogastrogram [4,6].

EGG dysrhythmias are associated with intestinal dysmotility and symptoms of nausea, vomiting, abdominal pain and bloating, and have been reported in a number of different conditions, most frequently in patients with gastroparesis [1,4,6,7]. Gastric electrical abnormalities have been demonstrated in children with delayed GE and GORD [8] and in children with CNS disorders who suffered from retching and/or vomiting [1]. Most patients with delayed GE and oesophagitis also had gastric dysrhythmia, suggesting that patients with more severe reflux, may have a more severe underlying motor dysfunction that is not restricted to the oesophagus, but extends throughout the foregut [1]. Del Giudice et al. reported that 67% of children with CP and GORD had delayed GE [9]. Concerning rate of GE, reports demonstrate that protein type in meals influences GE [10–13]. A mixture of 40% casein & 60% whey empties significantly faster than 100% casein [13], and postprandial symptoms occur more frequently with a fast emptying meal [14].

In the present study, the gastric myoelectrical pattern related to “fast and slow” GE in children with CP was recorded to reveal whether myoelectrical activity was influenced by type of meal or emptying rate. We also aimed to assess the association between EGG findings and gastrointestinal (GI) symptoms in this patient group.

2. Material and methods

2.1. Patients

Twenty children with CP and gastrostomy (9 females), ten of whom had been operated with a Nissen fundoplication (NF), and with a median age of 11 years (in both NF and non-NF group) (range 4–15 years) were recruited from five hospitals in the south of Norway (Oslo University Hospital, Ullevål, Akershus University Hospital, Østfold Hospital Trust, Vestfold Hospital Trust and Innlåntr Hospital Trust). Children with CP age below 16 years and have been reported in a number of different conditions, most often in patients with gastroparesis [1,4,6,7]. Gastric electrical abnormalities have been demonstrated in children with delayed GE and GORD [8] and in children with CNS disorders who suffered from retching and/or vomiting [1]. Most patients with delayed GE and oesophagitis also had gastric dysrhythmia, suggesting that patients with more severe reflux, may have a more severe underlying motor dysfunction that is not restricted to the oesophagus, but extends throughout the foregut [1]. Del Giudice et al. reported that 67% of children with CP and GORD had delayed GE [9]. Concerning rate of GE, reports demonstrate that protein type in meals influences GE [10–13]. A mixture of 40% casein & 60% whey empties significantly faster than 100% casein [13], and postprandial symptoms occur more frequently with a fast emptying meal [14].

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2.2. Experimental protocol

All patients were studied in the morning after an overnight fast on two consecutive days. The tests were performed at the outpatient/day-care ward. Prior to administration of the first test meal and the EGG recording, age, sex, height, weight, current feeding regimen and medications were recorded. Furthermore, history of symptoms of GORD, constipation and other GI symptoms were obtained and a history of previous abdominal surgery was recorded. After receiving the test meal and finishing the EGG recording, the children were allowed to perform their usual physical activity. No other meals were allowed during the test period with breath sampling. The children received their ordinary meal formulae between the test periods.

Postprandial GI symptoms occurring in the test period (4.5 h after meal administration) were recorded by the physician conducting the study (ACB).

2.3. Test meals

The main criterion for the selection of proteins for the test meals was that formulae with fast or slow proteins should be applied and the selected formulae should be commercially available. The meal formulae were made up of a standardized carbohydrate and fat base (Energivit (SIS), Liverpool, United Kingdom), which was added one of two protein sources (confer below) resulting in a meal formula containing a total energy of 1 kcal/ml with protein equivalent 2.8 g/100 ml, carbohydrate 12.0 g/100 ml and fat 4.5 g/100 ml. The protein sources were A) 100% casein and B) 40% casein/60% whey. The protein fractions were packed by a pharmacist and were blinded for the investigator and patients. 13C octanoic acid was added to the meal formula prior to administration. Meals were administered with a feeding pump, randomised and administered at a rate of 600 ml/h for 20 min (total 200 ml).

2.4. Gastric emptying (GE) – 13C breath test

The test meals were labelled with 91 mg 13C octanoic acid (EUROSO-TOP, Saint-Aubin Cedex, France) as a marker to measure the GE. The fraction of 13CO2 content in exhaled CO2 was determined by gas chromatographic purification isotope ratio mass spectrometry (Analytical Precision, Cheshire, UK). This technique is based on that GE is the rate-limiting step for the appearance of 13C in exhaled CO2 [16]. Three variables of GE were calculated; the halftime of GE (T1/2), the GE coefficient (GEC) and time until maximum excretion of 13C (Tmax) [17]. Prior to meal administration, a baseline breath sample was collected. Thereafter, breath samples were collected at 5 min intervals during the first 30 min after start of meal administration following by sampling at 15 min intervals for 4 h. In most cases, samples had to be collected through a face mask into a breath sampling bag (Quintron, Milwaukee, WI, USA) due to difficulties with breath sampling in the study patients. The sampling bag had a valve to avoid leaks.

2.5. Electrogastrography (EGG)

Gastric myoelectrical activity was measured using surface electrogastrography (GastroTrack, ElectroGastroGraphy, Alpine Biomed ApS, Skovlund, Denmark). The skin was cleaned and gently abraded with a paste (NuPrep Paste, Weaver and Company, Aurora, CO, USA) where the electrodes were to be placed. Then, an electrode cream was applied (Signa Conductive Gel, Parker laboratories, Fairfield, NJ, USA) in the abraded areas to improve signal transmission. Four paediatric active electrodes (EGG/EMG Electrode Small, 15 mm × 20, Alpine Biomed ApS, Skovlund, Denmark) were applied over the epigastrium following the antral axis of the stomach (Fig 1). A motion sensor was taped to the patient with some distance to the active electrodes to avoid interference. The program automatically controlled impedance for all channels. After appropriate patient preparation, a 30 min preprandial and a 60 min
Spearman’s correlation technique was applied to assess the correlation between gastric emptying variables (T1/2, GEC and Tmax) and EGG variables (ranges, dominant frequency instability coefficient (DFIC), dominant power instability coefficient (DPIC) and power ratio (PR)). Analyses were performed for both meals, and sub-analyses were performed for fast and slow “emptiers” within each meal group. In addition, sub-analyses were performed within the NF and non-NF groups. Summary values are given as mean and standard deviation (SD), unless otherwise stated. Wilcoxon test was applied to study differences between meals in emptying/EGG-variables due to a non-normal distribution. Student t-test was applied when comparing normogastria for children with and without NF. A p value of less than 0.05 was considered to indicate a statistically significant difference.

**Ethics**

Written, informed consents were obtained from the parents of all patients. The protocol was approved by the Regional Medical Ethics Committee and the Local data protection supervisor. The methods used are well known and do not imply risk or discomfort for the children.

**3. Results**

**3.1. Normogastria**

The expected increase in normogastria from preprandial to postprandial state was not observed for any meal. There was a significant decrease in normogastria from the preprandial state to the postprandial state after intake of meal B (p = 0.004, Fig. 2).

When comparing percentage normogastria for the children with and without NF, there were no significant differences between the groups.

**3.2. Power ratio**

The mean PR for meal A and B was 0.97 ± 1.60, and 1.16 ± 1.81, respectively (ns). For both meals, only 5 out of 20 patients (25%) had a PR > 1.

**3.3. Gastric emptying, EGG and symptoms**

For meal B (n = 20), there were significant correlations (p < 0.05) between T1/2 and PR (r = 0.55, p = 0.026) and T1/2 and DPIC post

**Fig. 2. Percentage slow wave distribution meal A and meal B.** Distribution of normal slow waves and dysrhythmia for meal A: 100% casein and meal B: 40% casein & 60% whey. There was a significantly lower percentage of postprandial normogastria for meal B than for meal A (p = 0.004), (Wilcoxon test). The expected increase in normogastria from preprandial to postprandial state was not observed for any meal. Values are mean ± SE, n = 20.

In the present study, particular attention was given to the two EGG variables commonly reported [4,6]: 1) Normogastria, reflecting the normal physiologic state, a measure of regularity of gastric SW recorded by EGG [5]. 2) PR, reflecting the ratio of the postprandial to fasting power which is normally > 1. A PR < 1 may imply a decreased distal gastric motor response to a meal [4,6].

[Textbox 1]

**Definitions of variables of electrogastrography (EGG).**

**Normogastria:** normal slow wave, 2–4 cycles pr.minute, (cpm).

**Brady gastria:** slow wave range, 0.5–2 cpm.

**Tachygastria:** slow wave range, 4–9 cpm.

**Power ratio (PR):** ratio between postprandial dominant power (DP) and preprandial DP.

**Instability coefficients:** this specifies the stability of the gastric electrical peak visible on the running spectra plot. It is the percentage ratio of the frequency standard deviation to the mean gastric frequency (DFIC) and the percentage ratio of the power standard deviation to the mean gastric power (DPIC).
(r = -0.48, p = 0.034) and between $T_{\text{max}}$ and PR ($r = 0.53$, $p = 0.037$) and $T_{\text{max}}$ and DPIC post ($r = -0.65$, $p < 0.01$), respectively (Table 1). There were no correlations between the variables of GE and EGG for meal A. No correlation was found between EGG variables and postprandial symptoms for any meal.

3.4. NF vs non-NF for meal B

For meal B, sub-analyses were performed for the NF ($n = 10$) and non-NF ($n = 10$) groups. There were no significant correlations for any group between variables of GE and EGG.

3.5. Slow vs fast gastric emptying

Sub-analyses were made for the 10 patients with fastest emptying within each meal, (meal A, $n = 10$, meal B, $n = 10$). No significant correlations were found between variables of GE and EGG.

4. Discussion

The present results demonstrate that the postprandial response to both “fast and slow” emptying meals is abnormal in children with CP. After meal intake, the percentage of EGG normogastria decreased, and only 25% of the patients had an increase in PR. The study compares variables of GE and EGG and correlations for $T_{1/2}$ and $T_{\text{max}}$ with PR and postprandial DPIC for the fast emptying meal was demonstrated. No correlations were found between EGG variables and GI symptoms.

Ravelli and Milla used EGG to study gastric motility in children with CNS disorders and found a variety of gastric dysrhythmias including both bradygastria and tachygastria [1]. Our aim was to record and analyse EGG findings in children with CP to evaluate the gastric myoelectrical pattern that accompanies “fast and slow” GE. We also aimed to assess the association between EGG findings and GI symptoms in this patient group. Food ingestion was not associated with induction or suppression of dysrhythmia in the study by Ravelli and Milla [1]. We found that normogastria was in the normal range in the preprandial stage (normogastria >70%), but the postprandial response to meals was abnormal with a decrease in normogastria. In healthy subjects, an increase in normogastria and PR is expected [4]. The differing preprandial results might be because Ravelli et al. had children with different CNS disorders and our patients were CP children only. The strength in our study is that Ravelli et al. had children with different CNS disorders and the meals were solid or solid-liquid, so these studies are also hard to compare. However, most studies find no correlation between GE and EGG. Correspondingly, in a recent paper by Yin et al. [6], it is emphasised that EGG measures SW, not contractions or emptying. Given the well-described foregut dysmotility in children with CP [9], a decrease in postprandial normogastria was not unexpected. However, it is not obvious why there was a greater drop in normogastria for the fast emptying meal (B) with 40% casein & 60% whey and why correlations between GE variables and PR were evident for this meal but not for the slow-emptying meal. The caloric content does not explain the difference but there are no studies that have compared the composition of the meal to evaluate the effect of caloric content on the GE.

Table 1

<table>
<thead>
<tr>
<th>GE</th>
<th>PR(^a) (r value)</th>
<th>p Value</th>
<th>DPIC post(^b) (r value)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$T_{1/2}$</td>
<td>0.55</td>
<td>0.026</td>
<td>-0.48</td>
<td>0.034</td>
</tr>
<tr>
<td>$T_{\text{max}}$</td>
<td>0.53</td>
<td>0.037</td>
<td>-0.65</td>
<td>0.002</td>
</tr>
</tbody>
</table>

\(^a\) $T_{1/2}$: time until half of the meal was emptied.

\(^b\) $T_{\text{max}}$: time until peak excretion of $^{13}$C.

\(^c\) PR: power ratio.

\(^d\) DPIC post: postprandial dominant power instability coefficient.

The lower postprandial normogastria is in line with previous results. Barbier et al. reported EGG recordings simultaneously with GE, but found no correlation between GE variables and EGG for a 500 kcal meal [21]. In a recent review it has been suggested that the test meal should contain a minimum of 250 kcal, with no more than 30% fat [6]. In our study we used liquid meals with 200 kcal. The volume and caloric content may not be sufficient, but as the studied objects were children with low body weight, and many had problems with larger volumes, this meal size was regarded appropriate.

The present study also compared various GE and EGG and correlations for $T_{1/2}$ and $T_{\text{max}}$ with PR and postprandial DPIC for the fast emptying meal with 40% casein & 60% whey were demonstrated. No correlations were found between EGG variables and GE of 100% casein or between EGG and GI symptoms. In adults, a correlation between EGG and GE has been reported in a number of studies. In the adult studies it seems to be a stronger relation between EGG results and GE than we found in our study, but they are hard to compare with the present data since we used liquid meals and an inclusion criteria which differs [22,23]. In paediatric patients with GORD, the postprandial change in GE dominant power has been reported to correlate with the type of GE of a solid-liquid meal measured with ultrasound [8]. However, other paediatric studies evaluating EGG recordings simultaneously with GE, report conflicting results. Barbier et al. reported EGG findings in four patients with normal scintiscans versus five patients with delayed GE of a solid meal and found no significant differences in the median PR or in the median difference in SW percentages in the preprandial and postprandial periods [24]. Riezzo et al. evaluated EGG with GE of a solid-liquid meal measured by ultrasound and found no correlation between the PR and the $T_{1/2}$ for GE [25]. Friessen et al. found no significant differences in EGG variables between patients with normal and delayed GE of a solid meal measured with ultrasound [26]. In the available paediatric studies [8,24–26], GE was measured with ultrasound or scintigraphy and the meals were solid or liquid-solid, so these studies are also hard to compare. However, most studies find no correlation between GE and EGG. Correspondingly, in a recent paper by Yin et al. [6], it is emphasised that EGG measures SW, not contractions or emptying.

Given the well-described foregut dysmotility in children with CP [9], a decrease in postprandial normogastria was not unexpected. However, it is not obvious why there was a greater drop in normogastria for the fast emptying meal (B) with 40% casein & 60% whey and why correlations between GE variables and PR were evident for this meal but not for the slow-emptying meal. The caloric content does not explain the difference but there are no studies that have compared the composition of the meal to evaluate the effect of caloric content on the GE.
activity, a pre-operative EGG should have been recorded, but this was beyond the scope of the current study.

The clinical relevance of our EGG finding is that in children with CP and gastrostomy, a pathological postprandial response to fast- and slow-emptying caloric liquid meals can be expected. A fast emptying meal might be unfavourable as normogastria dropped significantly. From our experience, EGG is an applicable test in most patient groups, even young children, and it would be of interest to study the effect of other types of meals as well, including regular food blended for use in gastrostomies.

To conclude, abnormal postprandial EGG recording seems to be common in children with CP and gastrostomy with both “fast and slow” protein meals. We found significant, but rather weak correlations between GE variables ($T_{1/2}$ and $T_{max}$) and EGG variables (PR and postprandial DPIC) for the fastest emptying meal with 40% casein & 60% whey. No relationship between EGG findings and GI symptoms was evident. In search for the right meal for the right patient, the present results may contribute, but further research evaluating various meals also over a prolonged period would be of interest. Furthermore, the results indicate that EGG may provide information in the diagnostic process of patients with complex diseases.

Statement of authorship

ACB participated in study design and wrote the study protocol, carried out the study, data analyses and wrote the manuscript. EJO participated in the EGG analyses. KS, GBJ and BSB participated in the study design and protocol, applied for initial funding and ethical approval. KS also helped to draft the manuscript. AWM participated in the study design and protocol, carried out data analyses and helped to draft the manuscript. All authors have given their final approval of the version to be submitted.

Funding

This project has been financially supported by the Norwegian Extra Foundation for Health and Rehabilitation through EXTRA funds. The study has also been supported by ESPEN Nutricia Research Fellowship Award 2005 and Vestfold Hospital Trust.

Funding made it possible for the corresponding author to carry out the present study and write the manuscript. The study sponsors had no involvement in study design, collection of data, analysis of data or writing of manuscript.

Conflict of interests

Anne Charlotte Brun has been an invited speaker at four paediatric meetings arranged by Nutricia.

Acknowledgements

The authors wish to thank pharmacist Kjersti Helland at the Hospital Pharmacy, Oslo University Hospital, Ullevål, for performing randomisation and preparing the liquid meals. Furthermore, the authors wish to thank Jarle Rugveit at the Paediatric Department, Oslo University Hospital, Ullevål, for valuable comments to the manuscript. We also wish to thank Ole Einar Smakasin at Vingmed AS, Norway, for technical EGG support.

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