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INVITED LECTURES

Electrogastrography in childhood

Alberto M Ravelli

Alberto M Ravelli, MD, Department of Pediatrics, University of Brescia, Italy

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Current understanding of the pathophysiology of gastrointestinal motility in the human infant and child is far from complete. This is largely due to the fact that invasive and unpleasant investigations are usually required to study contractile activity and transit through the gut. In fact, such invasive investigations are less acceptable and on average poorly tolerated by both infants and children, and therefore systematic studies are severely limited. The constraints imposed by such poor acceptability of extensive motility studies in childhood are the main reasons why pediatric gastroenterologists have become increasingly interested in non-invasive means of assessing gastrointestinal motility and transit. Such techniques include ultrasonography, breath test and electrical impedance tomography for the study of gastric emptying, and the recording of electrical activity of the gastric antrum by surface electrodes, *i.e.* electrogastrography or EGG.

From a historic point of view, EGG is not new in pediatrics. Back in 1926, in fact, four years after the first description of a human EGG by Walter Alvarez, I. Harrison Tumpeer, a pediatrician, published an article on the "registration of peristalsis by the Einthoven galvanometer"[1], and a few years later Tumpeer and Phillips reported the successful recording of an EGG from a 5 wk old infant with pyloric stenosis[2], who 'was so thin that gastric peris talsis was evident by simply watching the skin over his abdomen. It is noteworthy that this tracing (obtained by using standard ECG limb leads) was described by the Authors as looking like an ECG with a slowly changing baseline. The changes in the baseline clearly occurred at approximately 0.05 Hz and closely matched the frequency of gastric contractions that could be observed visually. Therefore Tumpeer and Phillips suggested that such ECG baseline changes, that had often been reported (but not explained) by cardiologist, were in fact due to gastric peristalsis. Since then, there were no further EGG studies in pediatric patients until 1978, when Telander *et al*[3] published a report describing a small infant with severe intractable vomiting and a marked impairment of gastric emptying. These abnormalities were related to a severe dysfunction of gastric smooth muscle, which in turn was due to a derangement of the frequency of gastric electrical control activity from the customary 3 cpm to a "tachygastria" of 4.7 cpm, and to an orad propagation of the electrical activity recorded in the gastric antrum. A similar patient with tachygastria underlying an intractable vomiting and the inability to assume oral feeds was described a few years later by Cucchiara *et al*[4]. In both these patients, antrectomy was curative of vomiting and gastroparesis, and allowed the children to resume oral feeds.

With time, the technique of recording and evaluation of the gastric electrical activity from surface electrodes has been considerably improved. The use of bipolar electrodes, adequate amplifiers and band-pass filters allows the recording of a much clearer signal. The digital conversion of the raw analogue signal at frequencies of 1-5 Hz provides a mathematical representation of the signal which is suitable for subsequent computerized analysis. The technique of running spectral analysis[5] (by Fast Fourier Transform, autoregressive modelling, or exponential distribution)[6]allows the frequency and power of the signal to be assessed in a more objective fashion than the simple visual inspection. Also, recent developments such as the wavelet analysis[7] can be used to remove artifacts and improve the interpretation of the re cording, especially in infants and young children. Such techniques are now customary in modern EGG, and were used in a number of pediatric EGG studies that have appeared in the literature over the last few years. Essentially, these studies were aimed at either defining the ontogenesis and development of gastric electrical control activity, or at investigating the role of gastric antral dysrhythmias in a number of pediatric disorders characterized by nausea, vomiting and feeding problems.

Koch *et al*[8] found a considerable degree of instability in the postprandial gastric electrical activity of both pre-term (28-32 wk) and term babies, with normal 2.5-3.6 cpm frequency occurring only for 9 to 34% of the time, and being often overwhelmed by frequencies within the bradygastria or tachygastria range. On the other hand, premature babies did not exhibit any increase in EGG power after gavage feeding of a standard low birth weight formula. These findings may reflect an immature response of the gastric neuromusculature (and also of the humoral control system) to formula feeds. Zacchi *et al*[10] described cyclic frequency and amplitude of the EGG signal in as many as 51% of infants. This is a common experience for pediatricians involved with gastrointestinal motility testing, and should be taken into account in order to avoid an overestimation of gastric dysrhythmias. By carrying out consecutive measurements of the EGG (at one week and two months), Liang *et al*[11] were able to describe a developmental pattern of gastric electrical activity in preterm infants, which was characterized by a significant increase in the percentage of 2-4 cpm activity and a reduction or normalization of tachygastria. Furthermore, by the age of 4.5 mo, fullterm infants

showed a significantly higher (70%) percentage of regular 3 cpm gastric slow waves in comparison with premature babies.

A number of EGG studies have been carried out in recent years in children with different disorders affecting all the control levels of gastrointestinal motor activity: Myogenic, neurogenic (intrinsic and extrinsic) and humoral. Devane *et al*[12] clearly showed that children with pseudo-obstruction related to a primary neuropathic disease had a persistent tachygastria. Several factors may account for the unstable electrical activity found in patients with myopathy: The inability to maintain a constant frequency or a poor summation of the electrical signal, due to a patchy involvement of smooth muscle cells in the disease process, or a marked reduction in signal amplitude and thus in signal-to-noise ratio. On the other hand, the most likely explanation for the tachygastria found in children with enteric neuropathy is a lack of intrinsic inhibitory innervation. Using techniques of chaos analysis, Bisset *et al*[13] were able to demonstrate the presence of complex high dimension interactions in the EGG of children with myopathic pseudo- obstruction, suggesting that gastric myocytes behave like other excitable cells, interacting in a chaotic manner that is increased by disease.

Severe recurrent vomiting, often complicated by aspiration and failure to thrive, is common in children with disorders of the central nervous system (CNS) such as cerebral palsy and psychomotor retardation. Vomiting is usually ascribed to gastroesophageal reflux, which indeed can be found in about 75% of these patients. In a group of 50 vomiting children with cerebral palsy and neurodevelopmental delay, 29 of whom had gastroesophageal reflux. Ravelli *et al*[14] showed that gastric dysrhythmias of different sorts (tachyarrhythmia, bradyarrhythmia, mixed dysrhythmia or unstable electrical activity) were as common as gastroesophageal reflux, occurring in 31 (62%) of the patients, and were associated with reflux in 1/3 of them. Furthermore, Ravelli *et al*[15] found that gastric dysrhythmias were present in most children with disorders of the CNS who had persistent r*etc*hing and postprandial discomfort following Nissen fundoplication, and were already present before the procedure was carried out. Thus it appears that children with CNS disease who suffer from recurrent vomiting often have a widespread disorder of foregut motility, where gastric dysrhythmias(possibly due to persistent activation of the emetic reflex) are as common as and may contribute to gastroesophageal reflux. In these children gastric dysrhythmias are probably due to abnormal modulation of the enteric nervous system by the CNS, although in some cases an involvement of the enteric nervous system by a process similar to that affecting the brain cannot be excluded. Since gastric dysrhythmias may be unmasked by Nissen fundoplication, EGG can be useful in detecting which patients are more likely to have r*etc*hing problems following this operation, so that in these patients alternative therapeutic interventions may be considered.

Gastric dysrhythmias have been described in adults with anorexia nervosa. In children with early onset anorexia nervosa, on the contrary, Ravelli *et al*[16] showed that the frequency of fasting and postprandial electrical activity and the fasting/postprandial amplitude ratio did not significantly differ from that of controls, although patients with longer established disease had a smaller increase in amplitude. It is therefore possible that gastric motility disturbances detected in adult patients with anorexia nervosa are related to a longer duration of the disease and are a consequence, rather than a cause, of malnutrition in these patients.

Different gastric dysrhythmias and delayed gastric emptying of a mixed solid-liquid meal were reported by Cucchiara *et al*[18] in a high proportion of children with non-ulcer dyspepsia[17]. In a few patients these alterations, together with the clinical symptoms, were successfully treated by the prokinetic drug cisapride. It is interesting to note that in adult patients with nonulcer dyspepsia, no significant correlation was found between gastric dysrhythmias detected by prolonged ambulatory EGG and the patients' symptom score.

A number of neuroamines (*e.g.* noradrenaline or dopamine) and polypeptide hormones (*e.g.* gastrin, glucagon, cholecystokinin) have the potential to induce gastric dysrhythmia, delayed gastric emptying, nausea and vomiting in humans. The effects of an altered humoral environment on gastrointestinal motility were investigated by Ravelli *et al*[19] in children with chronic renal failure. In a pilot study, children with chronic renal failure suffering from anorexia, nausea and vomiting were found to have dysmotility of the foregut in the form of gastroesophageal reflux, gastric dysrhythmia and/or altered gastric emptying. In most of them, serum levels of gastrin were increased above the upper normal limit. In subsequent studies, vomiting or anorectic children with chronic renal failure had significantly higher fasting and postprandial serum levels of gastrin, cholecystokin and neurotensin compared to asymptomatic uremic children and children who had undergone renal transplantation[20]. Gastric dysrhythmias, usually associated with delayed gastric emptying, were pre sent in 75% of symptomatic children with chronic renal failure, many of whom had gastroesophageal reflux on prolonged intraesophageal pH monitoring[20,21]. On the other hand, motility tests were normal in asymptomatic children with renal failure. Following renal transplantation, the gastric dysrhythmias disappeared in all patients in whom renal function and polypeptide hormone levels had normalized[20,21]. Thus it appears that gastric dysrhythmias (and gastroesophageal dysmotility in general) in chronic renal failure are related to an altered humoral environmrnt generated by the impaired renal degradation of these polypeptide hormones.

In summary, EGG can be safely and effectively used in pediatric patients, from premature babies to children and adolescents, to investigate the ontogenesis of gastric electrical activity and the pathophysiology of gastric dysrhythmias in a wide variety of disorders. In analogy to other aspects of gastrointestinal motility such as lower esophageal sphincter pressure and small intestinal motility, gastric antral electrical activity appears to develop from the prenatal period through the first few months of life. In normal healthy children, gastric electrical activity is similar to that in adults in terms of both frequency and response to a meal. Relevant abnormalities (gastric dysrhythmias) have been detected and characterized in several conditions where the different control levels of gastric motor activity are affected. Future developments such as electrical pacing, prolonged ambulatory EGG monitoring, chaos analysis and spatial mapping of gastric frequencies should render the EGG more and more meaningful for the study of gastrointestinal pathophysiology and the assessment of gastrointestinal disease.

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