

Original Articles

Erythromycin Improves Symptoms and Electrogastrographic Patterns of Children with Dyspepsia

MWY LEUNG, NSY CHAO, KKW LIU

Abstract

Purpose: Erythromycin is a prokinetic agent which enhances gastric smooth muscle contraction. In this study, we investigate the effect of short term erythromycin on children having dyspepsia symptoms. **Methods:** Eight children aged 7-18 with persistent dyspeptic symptoms were recruited. They all had abnormal dyspeptic symptom scores and electrogastrographic (EGG) patterns. All children were given erythromycin suspension 2 mg/kg thrice daily for 2 weeks. **Results:** All 8 children completed the 2-week course of erythromycin. Mean dyspepsia symptom scores before and after treatment were 6.75 and 4.63 respectively ($p=0.025$). Mean normogastria time in EGG before and after treatment were 65.87% and 77.58% respectively ($p=0.012$). After erythromycin, these eight children showed a significant difference between pre-prandial and post-prandial dominant power (46.00 dB vs 49.69 dB, $p=0.017$). None developed drug-related complication. **Conclusions:** EGG can demonstrate abnormal gastric myoelectrical activity in children having dyspeptic symptoms. Short-term erythromycin significantly improves the symptoms and EGG patterns of these patients.

Key words

Children; Dyspepsia; Electrogastrography; Erythromycin

Introduction

Functional dyspepsia is a common condition affecting children and adolescents.¹ The patients suffer from long history of upper abdominal pain with non-organic causes which are not related to defecation activities.² Associated symptoms include early satiety, postprandial abdominal

distension, nausea, vomiting and anorexia.^{3,4} The causes of functional dyspepsia are not well known and probably related to gastrointestinal dysmotility.^{5,6} Gastrointestinal dysmotility is also present in children with gastroesophageal reflux disease (GERD),⁷ malrotation of gut,⁸ oesophageal atresia⁹ and superior mesenteric artery (Wilkie's) syndrome.¹⁰ Electrogastrography (EGG) is a noninvasive technique to record and process the gastric myoelectric activity.¹¹ We have shown that abnormal EGG patterns occur more often in children with functional dyspepsia and gastrointestinal motility disorders comparing with controls.¹²

Erythromycin is a macrolide antibiotic. It is also a motilin agonist which enhances gastric smooth muscle contraction.¹³ It has been shown that intravenous erythromycin infusion promotes gastric emptying of liquid and solid food.¹⁴

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Methods

Study Design and Subjects

Eight children with age 7 to 18 (mean = 14.1) years old were recruited for the study. The inclusion criteria were

(1) children with functional dyspepsia or (2) GERD children with dyspepsia symptoms in spite of esomeprazole treatment. They all had dyspeptic symptoms for more than 6 months and abnormal EGG patterns. Six of them had functional dyspepsia. Preliminary blood and stool investigations were normal. Abdominal ultrasonography was done with normal findings. They had either upper gastrointestinal endoscopy or C¹³ urea breath test for *Helicobacter pylori* performed which was normal. Ambulatory 24-hour esophageal pH study was normal. Two children had GERD confirmed by 24-hour esophageal pH study with dyspeptic symptoms and delayed gastric emptying in spite of esomeprazole treatment at a dose of 20 mg daily. The baseline dyspepsia symptom score was assessed in these 8 patients. Six dyspeptic symptoms including upper abdominal discomfort, early satiety, post-prandial abdominal distension, nausea, vomiting and anorexia were described as none (grade 0), mild (grade 1), moderate (grade 2) and severe (grade 3). The total dyspepsia symptom score from 0 to 18 was charted.¹⁵

EGG Recordings

All children had baseline EGG performed. They were instructed to fast for 6 hours before the procedure. After skin preparation, four Ag/AgCl skin electrodes were applied to the upper abdominal wall at the gastric fundus, body, antrum and pylorus positions (Figure 1). Two additional electrodes were applied for grounding and reference purposes. After a pre-prandial EGG test for 30 minutes, a standard solid meal at 300 to 450 Kcal was given for 30 minutes. Then post-prandial EGG recording for another 60 minutes was done.¹⁶ The raw EGG signals were recorded and amplified by a multi-parametric recorder (Polygraf™ ID, Medtronic) and the data were subjected to customised analysis by the software (Polygram Net®, Medtronic) installed in an IBM-compatible personal computer. The frequency at which the EGG power spectrum had a peak power in the range of 0.5 to 9 cycles per minute (cpm) was defined as EGG dominant frequency. The power at the dominant frequency in the power spectrum was defined as the EGG dominant power. The normal EGG dominant frequency (normogastria) was defined as 2-4 cpm. Bradygastria referred to EGG dominant frequency below 2 cpm, and tachygastria meant EGG dominant frequency more than 4 cpm. Gastric dysrhythmia referred to no identifiable EGG dominant patterns.¹⁷ A normal EGG is defined as (i) normal gastric slow wave frequency at 2-4 cpm (normogastria) in over 70% of total recorded time; and (ii) the postprandial dominant power is greater than

the pre-prandial one (Figure 2).¹⁸

In these eight children with dyspeptic symptoms and abnormal baseline EGG results, erythromycin was given to them as a prokinetic treatment. Erythromycin ethylsuccinate oral suspension (200 mg in 5 ml) was prescribed to them with the dosage of 2 mg/Kg, up to a maximum dose of 100 mg thrice daily. The drug was given 30 minutes before meal. The erythromycin treatment was continued for 2 weeks. After that, they were called back for repeat assessment of dyspepsia symptom score and EGG test. In two patients with GERD, esomeprazole 20 mg daily was given during study period including the baseline and follow-up EGG tests.

Statistics

The dyspepsia symptom scores and EGG findings before and after erythromycin treatment were compared and analysed by Wilcoxon signed rank test. P value of 0.05 or less was considered to indicate statistical significance. The study was approved by the institutional review board of the hospitals.

Results

All 8 children completed the 2-week course of erythromycin. None of them developed drug-related complication. The dyspepsia symptom score pre-erythromycin treatment ranged from 3 to 11 (mean = 6.75).

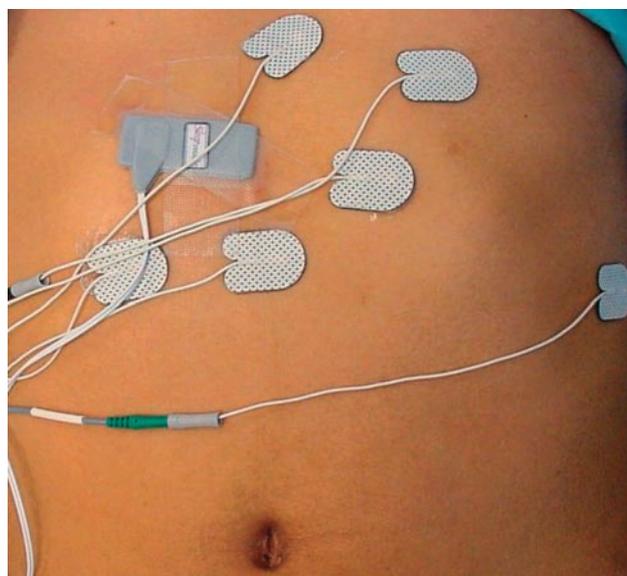


Figure 1 Electrogastrography skin electrodes.

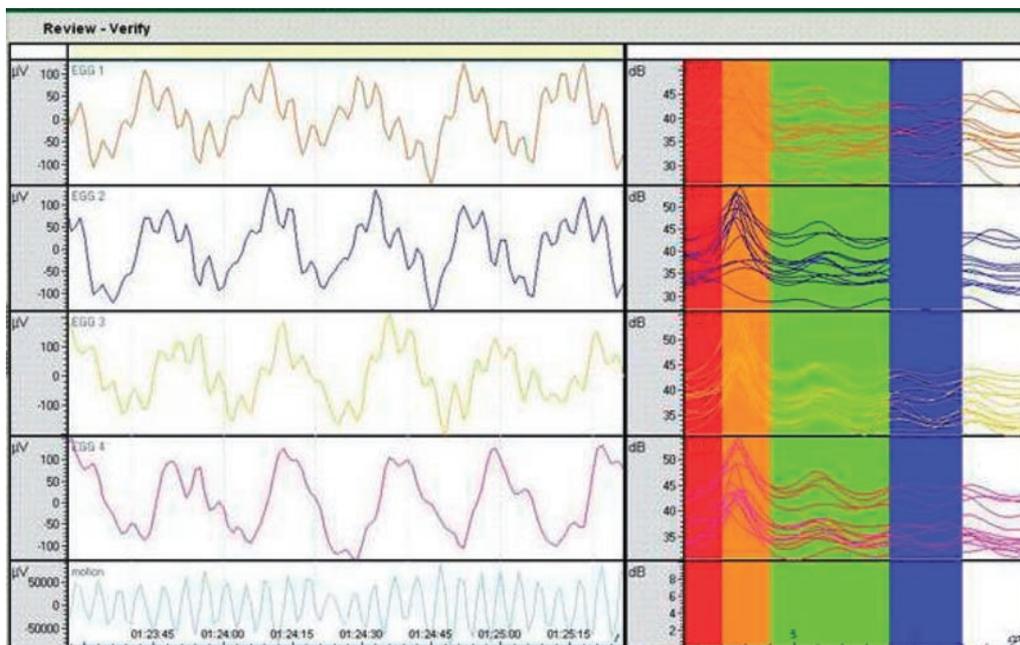


Figure 2 Normal electrogastrography.

After erythromycin treatment, six children had improvement of dyspepsia symptom score, one child had no change and one had a worsening score. The mean post-treatment score was 4.63. The difference in dyspepsia symptom score before and after erythromycin was statistically significant ($p=0.025$) (Table 1).

In these 8 children before erythromycin treatment, normogastric in EGG ranged from 52.13% to 82.12% of total recorded time (mean = 65.87%). In two children, the normogastric is over 70%. However, the dominant power was abnormal in these 2 children. One of them had post-prandial dominant power smaller than the preprandial one, and one patient had unidentifiable pre-prandial dominant power due to gastric dysrhythmia. Each patient had repeated electrogastrography performed after erythromycin treatment. All patients showed improvement in normogastric percentage. The mean post-treatment EGG normogastric of these children was 77.58%. The difference in EGG normogastric before and after erythromycin treatment was statistically significant ($p=0.012$) (Table 2).

Before erythromycin treatment, two children had pre-prandial gastric dysrhythmia such that the EGG dominant power could not be determined. The mean pre-prandial dominant power in the remaining 6 children was 43.80 dB. The mean post-prandial dominant power of these 8 children was 47.49 dB. There was no statistical difference between the pre- and post-prandial EGG dominant power before

erythromycin treatment ($p=0.25$). After erythromycin treatment, the mean pre-prandial dominant power of them was 46.00 dB and the mean post-prandial dominant power was 49.69 dB. There was a statistical significant difference between the pre- and post-prandial EGG dominant power after erythromycin treatment ($p=0.017$) (Table 3).

Discussion

Functional dyspepsia is a common problem in children and adolescents. The symptoms can severely affect the daily activities of the patients and yet all investigations are normal.¹⁹ There is some evidence that functional dyspepsia is related to gastrointestinal dysmotility. Some gastrointestinal motility disorder, such as GERD and intestinal malrotation, can present with symptoms similar to functional dyspepsia.

In a previous study, we have shown that abnormal EGG pattern occurred in 58.9% of children with functional dyspepsia, compared with only 12.5% in the control group ($p=0.042$). Also, children with known gastrointestinal motility disorder had a trend of increased abnormal EGG patterns.¹² The results are also compatible with studies by other workers.²⁰⁻²³

Cisapride and metoclopramide are traditional prokinetic agents for treatment of functional dyspepsia and

Table 1 Dyspepsia symptom scores before and after erythromycin treatment

Case	Sex	Diagnosis	Pre-erythromycin symptom score	Post-erythromycin symptom score
1	M	GERD	8	3
2	F	Functional dyspepsia	3	3
3	F	Functional dyspepsia	3	1
4	F	Functional dyspepsia	8	6
5	F	Functional dyspepsia	11	9
6	F	Functional dyspepsia	4	5
7	F	Functional dyspepsia	8	6
8	F	GERD	9	4
Mean symptoms score			6.75	4.63*

*Wilcoxon signed rank test p=0.025

GERD: gastroesophageal reflux disease

Table 2 Electrogastronomy nomogastric before and after erythromycin treatment

Case	Sex	Diagnosis	Pre-erythromycin normogastric (%)	Post-erythromycin normogastric (%)
1	M	GERD	52.13	71.79
2	F	Functional dyspepsia	82.12	89.09
3	F	Functional dyspepsia	68.57	80.51
4	F	Functional dyspepsia	59.38	73.93
5	F	Functional dyspepsia	69.73	70.17
6	F	Functional dyspepsia	70.03	78.09
7	F	Functional dyspepsia	56.04	71.20
8	F	GERD	68.97	85.88
Mean normogastric (%)			65.87	77.58*

*Wilcoxon signed rank test p=0.012

GERD: gastroesophageal reflux disease

Table 3 Electrogastronomy dominant power before and after erythromycin treatment

Case	Pre-erythromycin dominant power: (dB)		Post-erythromycin dominant power: (dB)	
	Pre-prandial	Post-prandial	Pre-prandial	Post-prandial
1	41.2	43.5	41.0	43.5
2	46.2	41.3	42.6	43.8
3	38.8	48.1	46.4	50.3
4	43.5	44.0	47.7	54.4
5	48.0	48.6	46.3	50.1
6	Not defined	57.6	46.8	54.4
7	45.1	49.0	42.9	42.7
8	Not defined	47.8	54.3	58.3
Mean	43.80	47.49	46.00	49.69*

* Wilcoxon signed rank test p=0.017

GERD: gastroesophageal reflux disease

gastrointestinal dysmotility. Use of cisapride has been discouraged because of the potential fatal cardiac complications.²⁴ The efficacy of metoclopramide is conflicting.^{25,26} Moreover, it can cause extra-pyramidal reactions.²⁷ Erythromycin, being a macrolide antibiotic, is also an agonist of motilin receptor on the antroduodenum which enhances enteric smooth muscle contractions. Numerous reports have supported the safety and efficacy of erythromycin as a prokinetic in neonates and infants.^{28,29} In the present study, we have shown that short term oral erythromycin suspension is a safe and well-tolerated prokinetic agent to be used in children with functional dyspepsia and GERD. All children completed the two-week treatment without side effects. The prokinetic dosage (6 mg/Kg/day) we used is smaller than the antibiotic dosage (30-50 mg/Kg/day). We believe a low dose regime should be used, because some side effects of erythromycin, such as gastrointestinal disturbance, may be dose dependent.³⁰

The dyspepsia symptom scores were improved in 6 out of 8 children (75.0%) after taking erythromycin for two weeks. However, the degree of improvement in symptoms was different and there was no improvement in two children (Table 1). There may be multiple causes for the different responses to erythromycin. Firstly, the symptom score is a clinical assessment by the patients themselves, which involved subjective variability. Also, erythromycin may relieve some dyspepsia symptoms (such as post-prandial abdominal distension) to a more extent than others. Moreover, it is not certain whether two-week treatment of erythromycin is adequate, or a longer period is necessary.

There are only few studies on electrogastrographic changes on children after erythromycin treatment.³¹ It has been shown that 4-week treatment of cisapride improved the post-prandial EGG dominant frequency in adult with non-ulcer dyspepsia.³² In our study, the EGG dominant frequency improved in all 8 children after erythromycin treatment. The mean normogastria improved from 65.87% to 77.58%. Erythromycin not only regulates the EGG dominant frequency, but also improves the EGG dominant power. It seems to enhance both pre-prandial and post-prandial EGG dominant power, though not statistically significant. The stronger gastric myoelectric activity after meal may be related to stronger antral smooth muscle contraction and subsequently better gastric emptying.³³ It was reported that acceleration of gastric emptying occurred after intravenous erythromycin infusion in healthy adults.³⁴

Dyspepsia is a heterogeneous condition. Gastric dysmotility is only one of the possible causes. The exact

relation of gastric dysmotility to dyspepsia symptoms is not clear. In some patients, improvement of EGG patterns may not correlated well with relieve of dyspepsia symptoms.

We admit that the sample size was small in this study. Moreover, the dyspepsia symptom score reported by the patients may be subjective and due to the placebo effect. In future, a larger scale prospective randomised controlled study should be performed.

In conclusion, short term low dose oral erythromycin suspension significantly improves the symptoms and electrogastrographic patterns of children with functional dyspepsia and gastroesophageal reflux disease. Electrogastrography, a non-invasive armamentarium, is useful in monitoring the progress of treatment. Further studies are indicated to investigate different dosages, durations and long term results of erythromycin treatment on children with functional dyspepsia and gastrointestinal motility disorders.

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