

Gastric and Colonic Myoelectrical Activity in Children with Overlapping Functional Dyspepsia and Irritable Bowel Syndrome

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Abstract

The article presents the results of a clinical study including 66 consecutive patients with FD-IBS overlap (functional dyspepsia-irritable bowel syndrome overlap) aged 10-15 years hospitalized to the Division of Pediatric Gastroenterology of the Municipal Children Clinical Hospital N°19, Kharkiv, Ukraine, for the treatment of functional dyspepsia (FD). Control Group comprised of 20 healthy coevals. Myoelectrical activity of the stomach and colon was investigated using non-invasive electrogastrography and electrocolonography. Fasting myoelectrical potential of the stomach (sMEP_f, mV), fasting and postprandial myoelectrical potential (cMEP_f and cMEP_p, mV) of the colon, and colonic postprandial response index cMEP_p/cMEP_f were evaluated.

It was determined that myoelectrical activity of the stomach and colon demonstrate predominantly unidirectional behavior in patients with low levels of fasting stomach myoelectrical potential. In particular, 77.8 ± 6.9% of patients with low sMEP_f had a similar type, namely, a hypo-reactive colonic myoelectrical response to a meal stimulation (cMEP_p/cMEP_f < 1.5). Incidence of average and hyper reactive postprandial colonic response in patients with low levels of sMEP_f was only 11.1 ± 5.2% each. While the incidence of average and hyper reactive postprandial colonic response in patients with average sMEP_f and low sMEP_f values was 30.0 ± 11.4% and 21.4 ± 10.9%, correspondingly.

However, the analysis of all registered types of myoelectrical activity of the stomach and colon has shown that the relations between the fasting stomach motility and colonic motility (in view of fasting colonic motility and postprandial colonic response) may be unidirectional, oppositely directed and uncorrelatable. Understanding oppositely directed and uncorrelatable myoelectrical behaviors of the stomach and colon is important for providing a more individualized approach to the treatment of patients with FD-IBS overlap.

Keywords: Gastric myoelectrical potential; Colonic myoelectrical potential; Postprandial colonic response; Gastrointestinal myoelectrical activity; Functional dyspepsia; Irritable bowel syndrome; Overlap; Children; Electrogastrography; Electrocolonography

Abbreviations: FD: Functional Dyspepsia; GI: Gastrointestinal; IBS: Irritable Bowel Disease; CMEP_f: Colonic Myoelectrical Potential (Fasting); CMEP_p: Colonic Myoelectrical Potential (Postprandial); MEP: Myoelectrical Potential; SMEP_f: Stomach Myoelectrical Potential (Fasting); SMEP_p: Stomach Myoelectrical Potential (Postprandial); CMEP_p/SMEP_f: Colonic Postprandial Response Index.

Background

Epidemiological studies of functional dyspepsia (FD) and irritable bowel syndrome (IBS) show that these conditions frequently coexist in adolescent patients (13–87%) [1,2]. Increased visceral sensitivity has been recognized as a primary pathophysiological mechanism of FD and IBS [3-5]. Motility of the upper and lower gut is closely related both on clinical and pathophysiological levels. For instance, clinically, IBS patients with constipation tend to more frequently present with postprandial fullness, early satiety, nausea, and other symptoms typical for delayed gastric emptying [3]. Noninvasive instrumental techniques, such as electrogastrography and electrocolonography, allow estimating condition of GI motility based on the levels of myoelectrical potential of the different parts of the GI tract.

Management of FD-IBS overlap is perplexing in the instances when the upper and lower gut motility exhibit an oppositely directed behavior:

e.g., hyper dynamic stomach associated with constipation, and delayed gastric emptying followed by IBS with diarrhea. For instance, use of prokinetics for the correction of congestive gastropathy associated with a hyper dynamic type of IBS may cause an excessive stimulation of colonic motility, and lead to an unpredicted clinical outcome. Since disturbances of GI myoelectrical activity are among the earliest mechanisms of the pathophysiological changes leading to the disorders of propulsive activity and functional diseases of the gut, therapeutic correction of the visceral hypersensitivity and normalization of the myoelectrical status of the stomach and intestine are a prospective treatment target for FD-IBS overlap. At the moment no clinical guidelines and recommendations on FD-IBS overlap with oppositely directed behavior of the upper and lower gut motility, are readily available. Thus, investigation of different types of myoelectrical behavior of the stomach and large intestine is important to develop individualized approaches to treatment of various types of FD-IBS overlap [5,6].

Objectives

The aim of the study was to investigate different patterns of gastric and colonic myoelectrical activity in children with FD-IBS overlap using electrogastrography and electrocolonography.

Materials and Methods

66 consecutive in-patients with FD-IBS overlap aged 10-15 years hospitalized to the Division of Pediatric Gastroenterology of the Municipal Children Clinical Hospital №19 were included in the study. Control Group comprised of 20 healthy coevals. There were 27 girls and 39 boys in the study Group. 18 patients with FD had constipation, 23 had diarrhea, and 25 had no stool disorders.

The Institutional Review Board and Ethics Committee at VN Karazin Kharkiv National University approved the study, and all patients and healthy volunteers gave their written informed consent. The study was performed in compliance with the ethical standards laid down in the 1975 Declaindexn of Helsinki.

The diagnoses of FD and IBS were established as per the Rome III Diagnostic Criteria [7] and confirmed by upper and lower endoscopy. Motility of the stomach and colon was investigated in all patients and controls using electrogastrography [8] and electrocolonography [9].

Myoelectrical activity of the stomach and colon was investigated by registering a total myoelectrical potential of these organs on the surface of the body. Stomach myoelectrical potential was registered once, in the morning, in the fasted state (fasting myoelectrical potential of the stomach (sMEP_f, mV)). Colonic myoelectrical activity was measured two times: in the fasted state in the morning, and postprandially, on the same day, in the afternoon, 30 minutes after a 500-calorie meal. Fasting and postprandial myoelectrical potential of the colon (cMEP_f and cMEP_p, mV) was registered, and cMEP_p/cMEP_f index was calculated to evaluate the after-meal activity of gastrocolic reflex, an essential part of the colonic propulsive activity [9].

Results

The parameters of physical development of children, included into the study, such as height and body weight, and body mass index were within 25-75 percentile. Body mass index (BMI) of the patients under study was within 5-85 percentile.

Levels of the fasting myoelectrical potential of the stomach (sMEP_f) were normally distributed in the control Group (standard skewness=0.79, standard kurtosis=-0.63), and varied from 0.14 to 0.18 mV, with M=0.158 ± 0.012 mV (Table 1). The values that exceeded 0.18 mV were considered to be above-average myoelectrical activity of the stomach in the study groups; and the values below 0.14 mV were estimated as below-average myoelectrical activity of the stomach.

Using the sMEP_f values of the controls as reference levels, the patients were divided into three study groups depending on the type of the fasting stomach myoelectrical potential: Group 1-patients with below average fasting myoelectrical potential of the stomach (sMEP_f<0.14 mV; n=36), Group 2-patients with average values of sMEP_f which varied from 0.14

to 0.18 mV, (n=16), and Group 3-patients with above average levels of sMEP_f exceeding 0.18 mV (n=14) (Table 1).

There was no statistically significant difference between the Group 2 with average values of fasting stomach myoelectrical potential and controls (p=0.58889 for the t-test comparison of means). There was a statistically significant difference between the Group 1 with below average sMEP_f and controls (p=0.00085 for the t-test). There was a statistically significant difference between the Group 3 and controls (p=0.000053 for the t-test).

We analyzed state of fasting and postprandial colonic myoelectrical potential in children with different fasting myoelectrical potential of the stomach. The values of the colonic fasting myoelectrical activity (cMEP_f) varied from 0.04 to 0.06 mV in controls, M=0.051 ± 0.009 mV. The values that exceeded 0.06 mV were referred to an above average myoelectrical activity of the colon, and the values below 0.04 mV were referred to a below average myoelectrical activity of the colon; the values of the cMEP_f that varied from 0.04 to 0.06 mV were referred to an average myoelectrical activity of the colon.

The values of the colonic index cMEP_p/cMEP_f reflecting the behavior of the myoelectrical activity after the meal stimulation varied from 1.5 to 2.0 in controls with M=1.58 ± 0.16. The values that exceeded 2.0 mV were considered to be a hyper-reactive, and the values below 1.5 mV - a hypo-reactive colonic myoelectrical response to a meal stimulation. These data commensurate with the previous studies [10]. Prevalence of different types of colonic myoelectrical activity in children with FD-IBS overlap is shown in figure 1.

It was revealed that the vast majority of children from Group 1 with below average stomach sMEP_f had a same-type (i.e., below average) colonic myoelectrical response to a meal stimulation (cMEP_p/cMEP_f<1.5 was

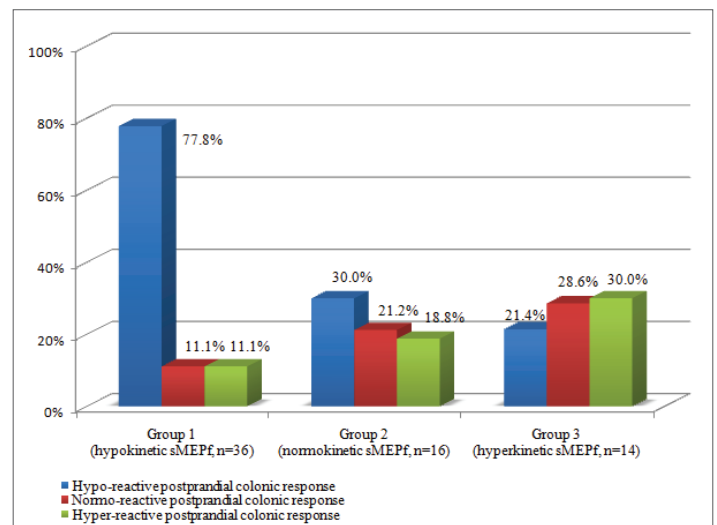


Figure 1: Occurrence of different types of postprandial colonic myoelectrical response (cMEP_p/cMEP_f) in children with FD-IBS overlap with hypo-, normo- and hyper-kinetic stomach myoelectrical activity (sMEP_f), %
*p<0.001 for the incidence of the hypo-reactive postprandial colonic response in Group 1 vs Group 2 and in Group 1 vs Group 3 (t-test)
**p<0.001 for the hypo-reactive postprandial colonic response Group 1 vs Group 3 (t-test)

Fasting myoelectrical potential of the stomach, sMEP _f , mV (M ± SD)	Group 1 (below-average sMEP _f , mV) n=36	Group 2 (average sMEP _f , mV) n=16	Group 3 (above average sMEP _f , mV) n=14	Controls (sMEP _f , mV) n=20
sMEP _f , mV (M ± SD)	0.103 ± 0.012*	0.155 ± 0.013**	0.236 ± 0.063***	0.158 ± 0.012 (0.14–0.18)

Table 1: Levels of fasting myoelectrical potential of the stomach in children with FD and IBS, sMEP_f, mV

* p_{1-control}=0.00085 for the t-test
** p_{2-control}=0.58889 for t-test
*** p_{3-control}=0.000053 for t-test

observed in $77.8 \pm 6.9\%$ of patients from Group 1; while the occurrence of both normo- and hyper-reactive postprandial colonic response reached only $11.1 \pm 5.2\%$; and in comparison with the Group 2 and 3 ($30.0 \pm 11.4\%$ and $21.4 \pm 10.9\%$, correspondingly) (Figure 1). In other words, myoelectrical activity of stomach and colon was largely co-directional in patients from Group 1, with below average $sMEP_f$. Patients from Group 3, characterized by above average fasting stomach myoelectrical potential $sMEP_f$, incidence of the hyper-reactive and normal postprandial colonic response (30.0 ± 12.2 and 28.6 ± 12.1) tended to be higher than the occurrence of the hypo-reactive postprandial colonic response (21.4 ± 10.9). However, the difference between these values did not reach the level of statistical significance.

The between-Group comparison of the incidence of the hyper-reactive colonic myoelectrical postprandial potential revealed that this type of myoelectrical activity was more frequent in patients with above average fasting stomach motility ($30.0 \pm 12.2\%$) than in the patients with average fasting stomach myoelectrical activity ($18.8 \pm 9.8\%$) and patients with below average fasting stomach myoelectrical activity ($11.1 \pm 5.2\%$); showing that the myoelectrical activity of the upper and the lower gut tend to be unidirectional in most instances; however, the differences between the groups were not statistically significant.

Analysis of the average values of the myoelectrical parameters of the stomach and colon showed that irrespective of the type of fasting stomach myoelectrical activity, the majority of children with FD-IBS overlap (59.1% , $n=39$) had average values of the fasting colonic myoelectrical potential, which decreased inversely after the meal stimulation ($cMEP_p/cMEP_f < 1$). Mean colonic response index $cMEP_p/cMEP_f$ of the patients in each study Group was significantly different from the values observed in controls (Table 2). The lowest average colonic response index $cMEP_p/cMEP_f$ was observed in Group 3 patients with above average $sMEP_f$ ($M=0.400 \pm 0.100$), compared to the groups with hypo-and average fasting stomach myoelectrical potential ($M=0.732 \pm 0.317$ and $M=0.694 \pm 0.383$, correspondingly). However, this difference did not reach statistical

significance, which could be a result of a small Group size, and this trend should be verified in larger samples. Comparison of the average values of the $cMEP_f$ in the study groups revealed no significant differences; while average values of these parameters did not differ from such in controls.

The normal postprandial colonic response was observed in 19.7% of study patients irrespective of the levels of the fasting stomach myoelectrical potential. While mean values of the fasting colonic myoelectrical potential $cMEP_f$ were significantly lower in groups 1 and 3 ($M=0.015 \pm 0.004$ and $M=0.03 \pm 0.018$, correspondingly) compared to controls ($M=0.051 \pm 0.009$) ($p < 0.05$) (Table 3). The lowest level of fasting colonic myoelectrical potential was observed in Group 1 patients who had the below average $sMEP_f$.

Thus, the above data show that the motility gradient reduction occurs in the caudal direction, and the below average levels of $sMEP_f$ are most often associated with below average levels of $cMEP_f$.

Above average colonic motility was observed in 21.2% of all study patients, showing the occurrence similar to the one of the normal colonic motility 19.7% , (Table 2). Mean levels of the colonic response index $cMEP_p/cMEP_f$ were significantly higher in all study groups than in controls (2.725 ± 0.330 ; 3.133 ± 1.185 ; 3.357 ± 0.985 for the groups 1, 2, 3, correspondingly, and 1.584 ± 0.154 for the controls, table 4). A statistically significant reduction of the fasting colonic myoelectrical potential $cMEP_f$ was observed in Group 1 with below average stomach $sMEP_f$ compared to the controls and to the Group 3 patients with above average stomach $sMEP_f$.

Discussion

Analysis of the study results revealed that FD-IBS patients with lower stomach $sMEP_f$ had a hypo-reactive postprandial colonic myoelectrical response (estimated by the colonic response index $cMEP_p/cMEP_f$) more frequently, than normo- and hyper-reactive types of colonic myoelectrical responses (77.1% vs 11.1% and 11.1% , correspondingly, figure 1). At the same time, the majority of children with an above average stomach $sMEP_f$ had a hyper-reactive postprandial colonic response compared to

Patients with hyporeactive postprandial colonic response from different study groups, n=39	Myoelectrical characteristics of stomach and colon		
	$sMEP_f$, M \pm SD, mV	$cMEP_f$, M \pm SD, mV	$cMEP_p/cMEP_f$, M \pm SD
Patients with hypo-reactive postprandial colonic response from Group 1 (below average $sMEP_f$), n=28	0.102 ± 0.024	0.050 ± 0.025	$0.732 \pm 0.317^*$
Patients with hypo-reactive postprandial colonic response from Group 2 (average $sMEP_f$), n=8	0.157 ± 0.012	0.048 ± 0.024	$0.694 \pm 0.383^*$
Patients with hypo-reactive postprandial colonic response from Group 3 (above average $sMEP_f$), n=3	0.277 ± 0.031	0.046 ± 0.007	$0.400 \pm 0.100^*$
Controls, n=20	0.158 ± 0.012	0.051 ± 0.009	1.58 ± 0.154

Table 2: Mean myoelectrical potentials of stomach and colon in patients with hypo-reactive postprandial colonic response from different study groups. * $p < 0.05$ colonic response MEP_p/MEP_f vs controls ($P_{1-controls} = 4.07631E^{-9}$ (t-test); $P_{2-controls} = 2.17734E^{-9}$ (t-test); $P_{3-controls} = 2.38209E^{-11}$ (t-test))

Patients with normo-reactive postprandial colonic response from different study groups, n=13	Myoelectrical characteristics of stomach and colon		
	$sMEP_f$, M \pm SD, mV	$cMEP_f$, M \pm SD, mV	$cMEP_p/cMEP_f$, M \pm SD
Patients with normo-reactive postprandial colonic response from Group 1 (below average $sMEP_f$), (n=4)	0.098 ± 0.033	$0.015 \pm 0.004^*, **$	1.900 ± 0.081
Patients with normo-reactive postprandial colonic response from Group 2 (average $sMEP_f$), (n=5)	0.148 ± 0.113	0.046 ± 0.013	1.770 ± 0.179
Patients with normo-reactive postprandial colonic response from Group 3 (above average $sMEP_f$), (n=4)	0.194 ± 0.011	$0.03 \pm 0.018^*$	1.675 ± 0.171
Controls, n=20	0.158 ± 0.012	0.051 ± 0.009	1.583 ± 0.154

Table 3: Mean myoelectrical characteristics of the stomach and colon in patients with normo-reactive postprandial colonic response from different study groups.

* $p < 0.05$ for the $cMEP_f$ vs controls ($P_{1-controls} = 0.0016$ (Kolmogorov-Smirnov test), $P_{3-controls} = 0.00143$ (t-test))

** $p < 0.05$ for the $cMEP_f$ Group 1 vs Group 2 ($P_{1-2} = 0.00296$ (t-test))

Patients with hyper-reactive postprandial colonic response from different study groups, n=14	Myoelectrical characteristics of stomach and colon		
	sMEP _f M ± SD, mV	cMEP _f M ± SD, mV	cMEP _p /cMEP _f M ± SD
Patients with hyper-reactive postprandial colonic response from Group 1 (below average sMEP _f), (n=4)	0.123 ± 0.010	0.028 ± 0.007*; **	2.725 ± 0.330***
Patients with hyper-reactive postprandial colonic response from Group 2 (average sMEP _f), (n=3)	0.163 ± 0.015	0.040 ± 0.026	3.133 ± 1.185***
Patients with hyper-reactive postprandial colonic response from Group 3 (above average sMEP _f), (n=7)	0.243 ± 0.079	0.051 ± 0.019	3.357 ± 0.985***
Controls, (n=20)	0.158 ± 0.012	0.051 ± 0.009	1.584 ± 0.154

Table 4: Mean myoelectrical characteristics of stomach and colon in patients with hyper-reactive postprandial colonic response from different study groups.

*p<0.05 for the cMEP_f vs controls (P_{1-controls}=0.0000521)

**p<0.05 for the cMEP_f vs Group 3 (P₁₋₃=0.0374105)

***p<0.05 for the colonic response index cMEP_p/cMEP_f vs controls (P_{1-controls}=0.00254527 (Kolmogorov- Smirnov); P_{2-controls}=0.00000267 (t-test); P_{3-control}=0.0000626954 (Kolmogorov- Smirnov))

below average and average colonic responses (30.0% vs 28.6 % and 21.4 %, correspondingly, figure 1). These observations show that stomach and colon generally tend to exhibit a unidirectional myoelectrical behavior. In such cases the use of the conventional therapeutic approach to treating abnormal motility in patients with FD-IBS overlap is recommended.

In the meantime, some patients with FD-IBS overlap had reverse patterns of myoelectrical activity of stomach and colon. For instance, some patients with *below average* stomach MEP had *above average* fasting colonic MEP, and, conversely, some patients with *above average* stomach myoelectrical potential had *below average* levels of the fasting colonic MEP (Table 4). Analysis of the mean values of the electrophysiological parameters of the gut in children with oppositely directed types of the upper and lower gut motility demonstrated that some children with below average fasting stomach myoelectrical activity had a hyper-reactive type of postprandial colonic response. At the same time the level of their fasting colonic potential was decreased, and a unidirectional type of myoelectrical activity of the stomach and colon was observed only in a fasting state, and changed after the meal intake (Table 4).

It is known that motility of different parts of the digestive tract is coordinated by locally active intramural pacemaker cells [11]. Gastric motility is coordinated by gastric pacemaker cells located along the greater curvature in the proximal to middle corpus and migrate in both circumferential and longitudinal directions; and the small intestine's motility is coordinated by the pacemaker, located in the proximal part of the duodenum. There is a physiological caudally directed gradient both of the main electrical rhythm, and of the rhythmic contractions of the smooth muscles of the gastrointestinal tube, which is present both in terms of frequency and the excitement conduction rate [12,13]. The speed of electric potential distribution varies in the different parts of the gut; it depends on the functional and morphological condition of the layers of the gastrointestinal wall, which impacts the pacemaker cells, and patterns of accumulation of static electricity [14,15]. Studies have demonstrated that under certain circumstances any part of the gastrointestinal tube can become a pacemaker for the more distal segments of the intestine [12]. Therefore, we can assume, that pathologically impaired electrophysiological processes in the stomach and colon may become uncoordinated, which may lead to oppositely directed behavior of the stomach and intestinal myoelectrical activity in patients with functional gastrointestinal disorders.

Thus, our study has demonstrated that patients with FD-IBS overlap may have different patterns of stomach and colonic myoelectrical behavior and can be unidirectional, oppositely directed and uncorrelatable. Any type of fasting stomach myoelectrical activity (hypo-, normo- or above average sMEP_f) may be accompanied by any kind of fasting and postprandial colonic activity (hypo-, normo- or above average colonic

response cMEP_p/cMEP_f). Hence, it is not always possible to predict a type of colonic myoelectrical activity based only on data of electrogastrography. It is recommended to perform both electrogastrography and electrocolonography testing in order to determine the type of stomach and colonic myoelectrical activity in patients with FD-IBS overlap [16,17]. Understanding and further investigation of mechanisms of oppositely directed and uncorrelatable behaviors of stomach and colon, and correlations between the myoelectrical patterns and clinical presentations of the stomach and colonic motility are important for the more personalized and targeted treatment of adolescents with FD-IBS overlap.

Conflict of Interest

The authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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