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Gastrointestinal Motility Disorders in Children

Prapun Aanpreung, M.D.*

Abstract : **From 1991 to 2000, thirty patients with gastrointestinal motility disorders were diagnosed in Department of Pediatrics, Siriraj Hospital. They were divided into 3 groups ; group 1, 15 patients had normal psychomotor development with chronic intestinal pseudo-obstruction (CIP) or intestinal dysmotility; group 2, 9 patients had psychomotor retardation with CIP or intestinal dysmotility and group 3, 6 patients had gastroparesis. Three cases in group 1 had underlying causes including megacystis-microcolon-intestinal-hypoperistalsis syndrome (MMIHS), SLE, and Strongyloid infestation. MMIHS was diagnosed during pregnancy, one of and the patient in this group did not respond to any medication and died at 5 months. Nine cases in group 2 and 1 case in group 1 were diagnosed as CIP due to their persistent symptoms of obstruction and radiologically demonstrated dilated intestine with air/fluid levels . The main presenting symptoms were abdominal distention (27 cases), constipation (14 cases), abdominal pain (13 cases), vomiting (9 cases), diarrhea (9 cases), and refusal of feeds (3 cases). X-ray studies were the most useful investigation to diagnose the disorders. All patients received cisapride as a prokinetic drug in order to improve the motility of the GI tract. A good response was obtained in 14 cases, a fair response in 15 cases and a poor response in 1 case. GI motility disorder is not uncommon in Thai children. The severity of the motility disorder varied from mild to severe. The majority of cases had a good prognosis except in the cases with psychomotor retardation.**

เรื่องย่อ : ภาวะการเคลื่อนไหวผิดปรกติของกระเพาะอาหารและลำไส้ในเด็ก

ประพันธ์ อ่านเปรื่อง, พ.บ.*
ภาควิชากุมารเวชศาสตร์, คณะแพทยศาสตร์ศิริราชพยาบาล, มหาวิทยาลัยมหิดล, กรุงเทพมหานคร 10700.

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**Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700.*

ในช่วงตั้งแต่ พ.ศ. 2534 ถึง พ.ศ. 2543 ภาควิชากุมารเวชศาสตร์ คณะแพทยศาสตร์ศิริราชพยาบาล พบผู้ป่วยเด็กที่ได้รับการวินิจฉัยว่ามีความผิดปรกติของการเคลื่อนไหวของกระเพาะอาหารและลำไส้ จำนวน 30 ราย แบ่งผู้ป่วยออกได้เป็น 3 กลุ่ม กลุ่มที่ 1 มีจำนวน 15 ราย เป็นผู้ป่วยที่มีพัฒนาการปรกติและได้รับการวินิจฉัยเป็น chronic intestinal pseudo-obstruction (CIP) หรือ intestinal dysmotility กลุ่มที่ 2 มีจำนวน 9 ราย เป็นผู้ป่วยที่มีปัญหาทางสมองและพัฒนาการช้า และได้รับการวินิจฉัยเป็น CIP หรือ intestinal dysmotility กลุ่มที่ 3 มีจำนวน 6 รายได้รับการวินิจฉัยเป็น gastroparesis ผู้ป่วย 3 รายในกลุ่มที่ 1 ทราบสาเหตุของโรคว่าเกิดจาก megacystis-microcolon-intestinal- hypoperistalsis syndrome(MMIHS), SLE, และติดเชื้อ Strongyloid ผู้ป่วย MMIHS 1 รายได้รับการวินิจฉัยตั้งแต่อยู่ในครรภ์ หลังคลอดผู้ป่วยมีอาการรุนแรง ไม่ตอบสนองต่อการรักษา และเสียชีวิตเมื่ออายุ 5 เดือน ผู้ป่วย10 รายได้รับการวินิจฉัย CIP เนื่องจากผู้ป่วยมีอาการรุนแรงและเรื้อรัง ภาพ X-ray แสดงให้เห็นว่ามีการขยายใหญ่ของลำไส้ร่วมกับ air fluid level

อาการที่พบ ประกอบด้วย ท้องอืด (27 ราย) ท้องผูก (14 ราย) ปวดท้อง (13 ราย) อาเจียน (9 ราย) อุจจาระร่วง (9 ราย) และปฏิเสธการกินอาหาร (3 ราย) การตรวจ X-ray มีประโยชน์ในการวินิจฉัยโรค ผู้ป่วยทุกรายได้รับยา cisapride เพื่อเพิ่มการเคลื่อนไหวของกระเพาะอาหารและลำไส้ ซึ่งได้ผลดี 14 ราย พอใช้ 15 ราย และไม่ดี 1 ราย ผู้ป่วยส่วนใหญ่จะมีอาการรุนแรงปานกลางและมีการพยากรณ์โรคดี ยกเว้นผู้ป่วยที่มีปัญหาทางสมองและพัฒนาการช้า

INTRODUCTION

Diseases of gastrointestinal dysmotility can be found in both children and adults such as gastroparesis, non-ulcer dyspepsia, pseudo-obstruction, constipation and neuromuscular disease of the colon[1]. GI dysmotility is resulted from disturbances of the control mechanism of gut motor activity, which may be produced by organic diseases involving enteric nerve, muscle, and altered central nervous system input. The main symptoms of GI dysmotility are recurrent vomiting, abdominal distention, abdominal pain, constipation and diarrhea. Gastroparesis is defined as delayed gastric emptying in the absence of demonstrable mechanical or mucosal lesion on radiographic or endoscopic studies[2]. Chronic intestinal pseudo-obstruction (CIP) is described as a rare, severe, disabling disorder characterized by repetitive episodes or continuous symptoms and signs of bowel obstruction, including radiographic demonstration of dilated bowel with air / fluid levels, and the absence of a fixed lumen occluding lesion[3]. However, in clinical practice, some patients have milder symptoms and bowel loops are not dilated or intermittently dilated. At the present time, there is still no specific term used to describe this. The term intestinal dysmotility will be used in this report.

In Thailand, few data concerning GI dysmotility in children have been reported[4,5], so the information is not widely known or accepted by general practice physicians. The objective of this study was to study the clinical manifestations, investigations, treatments and prognosis in children diagnosed with gastroparesis, CIP or intestinal dysmotility.

MATERIALS AND METHODS

The medical records of children with diagnosis of gastroparesis, CIP or intestinal dysmotility in Department of Pediatrics, Siriraj Hospital from 1991 to 2000 were retrospectively reviewed. Gastroparesis was diagnosed by demonstrating delayed gastric emptying without anatomical gut obstruction. The investigation showed a dilated stomach in plain abdominal X-ray or upper GI series or delayed gastric emptying study by scintigraphy method. In cases

of CIP and intestinal dysmotility, X-ray studies including plain abdominal film, GI follow through or barium enema demonstrated generalized dilatation of bowel without anatomical gut obstruction. The patients were divided into 3 groups ; group 1, patients with normal psychomotor development with CIP or intestinal dysmotility ; group 2, patients with psychomotor retardation with CIP or intestinal dysmotility; and group 3, patients with gastroparesis. Demographic data, clinical manifestation, investigation, treatment and prognosis were collected and analyzed. The results of treatment and prognosis were evaluated in 3 categories : 1) poor response or therapeutic failure; 2) fair response, indicating an improvement in symptoms, but still receiving a normal dose of medication; 3) good response, the symptoms had resolved completely or that the patient was on small doses of medication intermittently.

RESULTS

Thirty patients were enrolled in this study including 15 cases in group 1, 9 cases in group 2 and 6 cases in group 3. Their ages ranged from 1 day to 12 years. There were 19 female and 11 male patients. The description of patients are summarized in Table 1-3.

The presenting symptoms were abdominal distention (27 cases), constipation (14 cases), abdominal pain (13 cases), vomiting (9 cases), diarrhea (9 cases) and refusal to eat (3 cases) (Table 4). The investigation performed included plain abdominal X-ray (30 cases), GI follow through (16 cases), barium enema (12 cases), ultrasound (4 cases) and gastric emptying time study (4 cases) (Table 5). Treatment consisted of prokinetic drugs , antibiotics and total parenteral nutrition (Table 6). Antibiotics were used intermittently in some cases who had infection or bacterial overgrowth. All patients received cisapride as a prokinetic drug to improve bowel movement. There was a good response to cisapride in 14 cases, a fair response in 15 cases and a poor response in 1 case (Table 7).

In group 1, three underlying causes were identified including SLE, Strongyloid infestation and megacystis-microcolon-intestinal-hypoperistalsis syndrome (MMIHS). The case of MMIHS was diagnosed before delivery. Intra-abdominal cyst and bilateral hydronephrosis were detected by abdominal ultrasound during pregnancy. After birth, an exploratory laparotomy and investigation were performed which showed a dilated stomach, hydronephrosis, hydroureter and a dilated urinary bladder. The patient did not respond to cisapride, erythromycin or octreotide. She died after 5 months. The remaining patients had good or fair response to treatment.

In group 2, six out of nine patients came from the Pak-kred Home for Mentally and Physically Handicapped Babies. All patients had persistent symptoms especially abdominal distention but did not need total parenteral nutrition (TPN), so CIP was diagnosed in these patients. In group 3, the underlying cause of gastroparesis could not be identified, but all patients had a good prognosis.

DISCUSSION

Pseudo-obstruction may be resulted from any process that interferes with the coordinated patterns of propulsive motor activity and normal intestinal transit. It may be acute or chronic in nature. The chronic disorders are divided into primary disorders of intestinal smooth muscle or the myenteric plexus and secondary systemic illnesses affecting gastrointestinal neural and muscular functions. Secondary disorders in children such as infection, drug, endocrine and metabolic disorders are not common[6]. In a survey for children with pseudo-obstruction conducted by members of the North American Society of Pediatric Gastroenterology and Nutrition in 1988, 22 percent of 87 identified cases had symptoms at birth, 43 percent within the first month, and 64 percent in the first year of life. One third of infants born with CIP died in the first year of life[7]. This high mortality can be explained by the interaction of several complicating factors. About one third of CIP infants had associated neuromuscular disease of bladder. These infants may be at high risk for recurrent urinary tract infection.

In a previous study, Varavithya W reported 14 Thai children with CIP. Nine cases had onset of symptoms after birth including Waardenberg syndrome (2 cases), MMIHS (3 cases) and unknown causes (4 cases). Five cases died and three cases

Table 1. The descriptive data of patients in group 1.

Case	Age	Underlying disease	Duration of symptom	Investigation	Treatment	Response	Duration of follow-up
1	1 D	MMIHS	1 D	upper GI series, abdominal ultrasound, VCUG	cisapride erythromycin, octreotide, TPN	poor	5 M
2	1 D	Normal child	1 D	GI follow through, barium enema, gastric emptying	cisapride	good	5 M
3	1 M	Normal child	1 M	GI follow through, barium enema	cisapride, octreotide, TPN	good	4 Y
4	1.3 Y	Normal child	7 M	plain abdomen	cisapride	good	2 M
5	2.3 Y	Normal child	1 M	GI follow through, abdominal ultrasound	cisapride, metronidazole	good	5 M
6	3 Y	Normal child	3 M	GI follow through, barium enema, gastric emptying	cisapride	fair	10 M
7	3 Y	Normal child	2 Y	plain abdomen	cisapride	fair	6 M
8	4 Y	Normal child	1 Y	plain abdomen	cisapride	good	6 M
9	4 Y	Normal child	1 Y	plain abdomen	cisapride, mineral oil	fair	6 M
10	4.5 Y	Normal child	4.5 Y	barium enema	cisapride, mineral oil	good	5 Y
11	5 Y	Strongyloid infestation	1 M	GI follow through	cisapride, erythromycin, thiabendazole	good	5 M
12	5.6 Y	Normal child	1 Y	barium enema	cisapride, mineral oil	good	3 Y
13	5.9 Y	Normal child	2 M	GI follow through	cisapride	good	3 Y
14	8 Y	Normal child	3 M	GI follow through, barium enema	cisapride metronidazole	fair	3 M
15	12 Y	SLE	0.5 M	CT abdomen, colonoscopy	cisapride, erythromycin, metronidazole, prednisolone	good	9 M

VCUG = voiding cystourethrography

Table 2. Descriptive data of patients in group 2.

Case	Age	Duration of symptom	Investigation	Treatment	Response	Duration of follow-up
1	2 Y	unknown	plain abdomen	cisapride, metronidazole	fair	2.5 Y
2	2.8 Y	5 M	plain abdomen	cisapride	fair	1.3 Y
3	5 Y	unknown	barium enema	cisapride, erythromycin, metronidazole	fair	1.2 Y
4	6 Y	unknown	GI follow through, barium enema, gastric emptying	cisapride, metronidazole	fair	7 M
5	8.5 Y	3 Y	GI follow through, barium enema	cisapride, mineral oil	fair	1 M
6	8.5 Y	3 Y	GI follow through, barium enema	cisapride, mineral oil	fair	1 M
7	8.5 Y	unknown	barium enema,	cisapride	fair	6 M
8	11 Y	unknown	GI follow through, barium enema, gastric emptying	cisapride	fair	6 M
9	11 Y	unknown	barium enema	cisapride	fair	3.5 Y

Table 3. Descriptive data of patients in group 3.

Case	Age	Duration of symptom	Investigation	Treatment	Response	Duration of follow-up
1	3.7 Y	3 M	GI follow through	cisapride, erythromycin	good	4 M
2	4 Y	4 Y	GI follow through	cisapride	good	3 M
3	5 Y	2 Y	GI follow through	cisapride	fair	1 Y
4	6.5 Y	0.7 M	GI follow through	cisapride	good	1 Y
5	7 Y	1 Y	plain abdomen	cisapride	fair	3 M
6	7 Y	3 M	plain abdomen	cisapride	good	3 M

Table 4. Presenting symptoms of patients.

Symptom	Group 1 (case)	Group 2 (case)	Group 3 (case)	Total (case)
Abdominal distention	15	9	3	27
Constipation	9	5	-	14
Abdominal pain	9	-	4	13
Diarrhea	4	5	-	9
Vomiting	6	-	3	9
Refusal of feeding	-	-	3	3

Table 5. Investigations performed in patients.

Investigation	Group 1 (case)	Group 2 (case)	Group 3 (case)	Total (case)
Plain abdomen	15	9	6	30
GI follow through	8	4	4	16
Barium enema	5	7	-	12
Ultrasound	2	2	-	4
Gastric emptying	2	2	-	4
CT abdomen	1	-	-	1
Colonoscopy	1	-	-	1
VCUG	1	-	-	1

VCUG = voiding cystourethrography

Table 6. Treatments in patients.

Medication	Group 1 (case)	Group 2 (case)	Group 3 (case)	Total (case)
Cisapride	15	9	6	30
Erythromycin	3	1	1	5
Octreotide	2	-	-	2
Metronidazole	3	3	-	6
Mineral oil	3	2	-	5
TPN	3	-	-	3

Table 7. Response of treatments.

Response	Group 1 (case)	Group 2 (case)	Group 3 (case)	Total (case)
Good	10	-	4	14
Fair	4	9	2	15
Poor	1	-	-	1

needed TPN. Another case could take food orally. The other 5 cases had symptoms which developed after neonatal period. Their symptoms and signs resolved within 6-12 months. In this study, only 10 cases of gastrointestinal dysmotility were diagnosed as CIP. MMIHS which is the most severe form of this disease was found in one case. Six patients came from Pak-kred Home for Mentally and Physically Handicapped Babies, so the timing of the onset of symptoms could not be achieved. We could not conclude whether the diagnosis was a primary or secondary disorder in these patients. The causes of GI dysmotility may arise from abnormalities in the intestinal muscle, peripheral and central nervous system, malnutrition, electrolyte imbalance, infection and aerophagia. These patients needed NG tube feeding, intermittent oral metronida-zole and mineral oil, and high doses of cisapride. Symptoms were mildly or moderately improved, and the patients did not need long- term TPN.

MMIHS is the most severe form of pseudo-obstruction which predominantly affects female infants. In most cases, it can be detected by prenatal ultrasound scan showing megacystis, hydronephrosis and/or gastric distention. The syndrome is identified by marked, non-obstructive bladder enlargement, dilated and peristaltic proximal small bowel, narrowed distal small bowel and a malrotated microcolon located entirely on the left side of the abdomen. It is usually caused by a myopathy with vacuolar degenerative change of smooth muscle cells, this phenotype can also be a manifestation of neuropathy. After birth, the children develop massive abdominal distention which is often relieved when a huge bladder is catheterized. The prognosis is poor because there is no effective medical treatment. Most children die within the first year of life due to renal insufficiency, postoperative complication or sepsis[8].

In clinical practice, many patients come to see the doctors because of intermittent or persistent vomiting, abdominal pain, abdominal distention and constipation but the symptoms are not extremely severe. Gastroparesis and intestinal dysmotility are likely to be the diagnoses in these patients. The underlying cause for the majority of patients in group 1 (except 3 cases) could not be found. However, they responded to treatment with cisapride. Ten cases were able to discontinue cisapride with completely resolved symptoms.

Signs and symptoms of gastroparesis include nausea, vomiting, abdominal distention and epigastric pain, early satiety, belching in older children and regurgitation, irritability, food refusal and failure to thrive in infants and toddlers. Vomiting many hours after eating suggests a diagnosis of gastroparesis, especially if the vomitus contains recognizable foods[9]. The physiology responsible for gastroparesis may include reduced contraction in the stomach, failure of relaxation of the duodenum, impaired co-ordination between stomach, pylorus, and duodenum, or a combination of these factors. The etiologies of gastroparesis include anatomical obstruction, metabolic or electrolyte disorder, drug, neuronal dysfunction, muscle disease and infection[10]. In group 3, refusal of feeding was the only symptom seen in cases of gastroparesis. Although the underlying causes of gastroparesis could not be determined, their prognosis was good.

X-ray studies are the useful investigations in the diagnosis of GI dysmotility. The pattern of gas in the GI tract seen in a plain abdominal film gives an idea whether further X-ray investigations

are necessary. There were 8 cases who had only a plain abdominal X-ray performed because their history, symptoms and signs did not suggest evidence of anatomical gut obstruction. Gastrointestinal manometry study is the best investigation to diagnose GI dysmotility. Besides requiring an expensive machine, it is a difficult technique and needs a well trained physician to perform it. These factors limit its use. X-ray contrast studies are also helpful as these will give some information about gastrointestinal transit time and can exclude anatomical obstruction. Another motility study is gastric emptying study using radioactive substance. It demonstrated delayed gastric emptying in all 4 cases in group 1 and 2.

Treatment is symptomatic and supportive in all primary and secondary causes of intestinal dysmotility, unless the underlying diseases process can be corrected by specific treatment. Nutritional therapy plays an important part . The enteral feeding route should always be preferred to parenteral nutrition if possible. Even small volumes of enteral feeding maintain bowel mucosal integrity and the secretion of mucosal-derived gastrointestinal hormone and decrease the risk for bacterial translocation, sepsis, and cholestatic liver disease. In this report, there was only one case of MMIHS receiving long term TPN and 3 cases needing temporary TPN.

Bacterial overgrowth frequently occurs in a non-propulsive small bowel, and further enhances malabsorption and bowel dilatation due to fermentation of carbohydrate. Intermittent treatment with non-absorbable antibiotic is recommended and often improves symptoms and stool pattern. Six cases received metronidazole to treat suspected bacterial overgrowth due to persistent diarrhea or progressive abdominal distention unresponsive to prokinetic drugs.

Improved intestinal motility by prokinetic agents can only be expected if there is some remaining function of enteric nerve and muscle. Cisapride may improve motility and symptoms in mild to moderate primary and secondary neuromuscular intestinal diseases[11,12]. It binds to serotonin receptor on the motor nerve of myenteric plexus, facilitating release of acetylcholine, and stimulating gastrointestinal smooth muscle contraction. The response seems better if there is no associated autonomic dysfunction. In this study, cisapride is the main prokinetic drug with a fair to good response. Erythromycin acts as a motilin agonist by binding to motilin receptors on smooth muscle in the stomach and intestine[13,14]. Studies in adults and children have demonstrated improvement of gastroduodenal motility and gastric emptying in healthy humans and those with diseases[15-17]. Because intravenous erythromycin is available, it is frequently used in patients who do not tolerate oral medication initially. Five cases in this study received intravenous or oral erythromycin with good results.

Surgical intervention should be reserved for patients with severe symptoms. Bowel resection is only helpful in patients with the disease limited to specific parts of the colon or a short segment of the small intestine. Gastrostomy and jejunostomy are often necessary for feeding and decompression. A venting ostomy in the small or large bowel may be considered if abdominal pain and vomiting deteriorate. However, there was no patient undertaking surgical intervention in this report.

In conclusion, thirty children with GI dysmotility were presented including those with a diagnosis of gastroparesis, CIP and intestinal dysmotility. The majority of cases had a good or fair response to oral cisapride. There was one case of CIP diagnosed as MMIHS who had severe symptoms and died. The severity of the other cases varied from mild to severe. The majority of cases had a good prognosis except those who also had psychomotor retardation.

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