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Prospective Study**Gastrointestinal contrast-enhanced ultrasonography for diagnosis and treatment of peptic ulcer in children**

Gastrointestinal contrast-enhanced ultrasonography of peptic ulcer

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Abstract**BACKGROUND**

The detection rate of peptic ulcer in children is improving, with development of diagnostic procedures. Gastroscopy is the gold standard for the diagnosis of peptic ulcer, but it is an invasive procedure. Gastrointestinal contrast-enhanced ultrasonography has the advantages of being painless, noninvasive, nonradioactive, easy to use, and safe.

AIM

To investigate the clinical value of contrast-enhanced ultrasonography (CEUS) for diagnosis and treatment of peptic ulcer in children.

METHODS

We investigated 43 children with digestive tract symptoms in our hospital from January 2021 to June 2022. All children were examined by routine ultrasound, gastrointestinal CEUS, and gastroscopy. The pathological results of gastroscopy were taken as the gold standard. Routine ultrasonography was performed before gastrointestinal CEUS.

Conventional ultrasound showed the thickness of the gastroduodenal wall, gastric peristalsis, and the adjacent organs and tissues around the abdominal cavity. Gastrointestinal CEUS recorded the thickness of the gastroduodenal wall; the size, location and shape of the ulcer; gastric peristalsis; and adjacent organs and tissues around the abdominal cavity. The results of routine ultrasound and gastrointestinal ultrasound were compared with those of gastroscopy to evaluate the diagnostic results and coincidence rate of routine ultrasound and gastrointestinal CEUS. All children received oral informed consent from their guardians for CEUS. This study was reviewed and approved by the hospital medical ethics committee.

RESULTS

Among the 43 children, 17 (15 male, 2 female) were diagnosed with peptic ulcer by gastroscopy. There were 26 children with nonpeptic ulcer. There were eight cases of peptic ulcer and 35 of nonpeptic ulcer diagnosed by conventional ultrasound. The diagnostic coincidence rate of peptic ulcer in children diagnosed by conventional ultrasound was 79.1% (34/43), which was significantly different from that of gastroscopy ($P = 0.033$). It indicates that the coincidence rate of gastrointestinal contrast-enhanced ultrasound and gastroscopy is low. Fifteen cases of peptic ulcer and 28 of nonpeptic ulcer were diagnosed by CEUS. The diagnostic coincidence rate of peptic ulcer in children was 95.3% (41/43). There was no significant difference between CEUS and gastroscopy ($P = 0.655$). It indicates that the coincidence rate of gastrointestinal contrast-enhanced ultrasound and gastroscopy is high.

CONCLUSION

Gastrointestinal CEUS has a high coincidence rate in the diagnosis of peptic ulcer in children, and can be used as a preliminary examination method.

Key Words: Contrast-enhanced ultrasound; Peptic ulcer; Children; Gastrointestinal tract; Abdominal pain; Acoustic contrast agent

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Core Tip: In this study, routine gastrointestinal ultrasound and contrast-enhanced ultrasound (CEUS) in children were compared with gastroscopy. The clinical coincidence rate between gastrointestinal CEUS and gastroscopy was higher, which provided a new examination method for pediatricians to screen upper gastrointestinal diseases. This method is painless, noninvasive, nonradioactive, simple to operate, accepted by children and parents, and can be used as a preliminary screening method for children with epigastric pain. It is expected to be an effective supplement to gastroscopy and provide a reference for clinical selection of appropriate treatment.

INTRODUCTION

Gastrointestinal CEUS in children has high accuracy, which provides pediatricians with a new and simple method for screening upper gastrointestinal diseases in children, which is easily accepted by children and parents, and is an effective supplement to gastroscopy. For children with recurrent abdominal pain and other upper gastrointestinal symptoms with unknown etiology, gastrointestinal CEUS should be performed to provide a reference for clinical selection of appropriate treatment.

MATERIALS AND METHODS

Peptic ulcer refers to chronic ulcer in the stomach and duodenum. It is a common disease in adults that is mainly caused by the erosion of gastrointestinal mucosa by gastric acid and pepsin. In the past, it was considered that peptic ulcer was rare in children, but the development of diagnostic procedures has increased detection rates continuously. The lifetime prevalence rate of peptic ulcer in the general population is 5%–10%, with an annual incidence rate of 0.1%–0.3%^[5]. Peptic ulcer in children is caused by many factors. The common cause is *H. pylori* infection. Oral and fecal

transmission is the main route. *H. pylori* infection is mainly acquired in childhood, and adults can transmit *H. pylori* to children. *H. pylori* infection is still highly prevalent in children and adolescents globally^[6]. In this study, the number of children with *H. pylori* infection was 88%. Overseas studies have also shown that *H. pylori* is the main cause of peptic ulcer, and > 75% of duodenal ulcers and > 17% of gastric ulcers are associated with this infection^[7]. In children with *H. pylori*-infected duodenal ulcers, the mucosal microbiota of the duodenal bulb is altered, characterized by an increased abundance of *Helicobacter* and decreased abundance of *Clostridium* and *Streptococcus*, which possibly alters the biological function of the commensal microbiota through specific metabolic pathways^[8]. A systematic review and meta-analysis that assessed the global prevalence of *H. pylori* infection found that more than half the population is infected^[9]. Therefore, it is essential to develop a plan for early detection of *H. pylori* to reduce the risk of peptic ulcer^[10].

In our study, there were more male than female children with peptic ulcer, which is consistent with a previous study^[11]. This may be because boys exercise more, eat too much and eat fast, which leads to excessive and rapid gastric acid secretion, which in turn destroys the duodenal mucosal barrier. Girls have higher estrogen levels, which can stimulate the duodenal mucosa to secrete bicarbonate, enhance mucosal barrier function, inhibit gastric and duodenal juice secretion, and reduce pepsin activity, thus protecting gastrointestinal mucosa to reduce the occurrence of ulcers^[12, 13].

The clinical symptoms of peptic ulcer in children vary with age. Studies have shown that younger children may be irritable, eat a poor diet, and have gastroesophageal reflux but no significant weight gain, and older children may be characterized by abdominal pain, flatulence, hematemesis and black stools^[14]. In this study, all children had varying degrees of abdominal pain, because most children cannot accurately describe the degree, location and duration of abdominal pain, it is easy to miss diagnosis or misdiagnose, resulting in delayed treatment, seriously affecting the health of children. Moreover, the proportion of perforation, massive hemorrhage, severe anemia and other serious complications of peptic ulcer in children

is higher than in adults^[15, 16]. It has been reported that most cases of duodenal ulcer perforation are in teenagers; less than half the cases have a history of abdominal pain, and most of them have ulcer perforation at the beginning of acute disease, which may be related to the inability of children to accurately describe abdominal discomfort^[17].

The results of gastroscopy are used as the gold standard for the diagnosis of peptic ulcer in children. However, gastroscopy is an invasive examination method. Because the anatomical structure of the upper digestive tract in children is different from that in adults, it is difficult to operate with the narrow gastrointestinal tract and thin gastrointestinal wall, and cooperation from children is difficult. It is reported that only 55% of children with gastrointestinal symptoms have abnormal gastroscopy results^[18]. Age is also a risk factor for children in capsule endoscopy^[19]. Children do not cooperate well with ordinary gastroscopy, and even painless electronic gastroscopy may have adverse reactions such as hypotension, myocardial ischemia, drug allergy, and arrhythmia. Therefore, ultrasound as a safe, simple, noninvasive and rapid examination method for screening peptic ulcer in children is particularly important. Due to the presence of intestinal gases and feces, the diagnostic quality of conventional gastrointestinal ultrasound may be affected, and the diagnostic sensitivity is lower in older or obese children. Gastrointestinal CEUS can eliminate the interference of gas and contents in the gastrointestinal cavity and improve the diagnostic value of gastroduodenal diseases by filling the gastrointestinal cavity with oral contrast agent.

A total of 43 children were included in this study; 17 cases of duodenal ulcer were diagnosed by gastroscopy, and eight cases were diagnosed by routine ultrasound. The diagnostic accuracy was 47.1% (8/17), and the coincidence rate was 79.1% (34/43). Ultrasonography showed thickening of the local intestinal wall of the duodenum, decreased echo, stiffness and decreased peristalsis. Routine gastrointestinal ultrasound has some limitations, and the coincidence rate of diagnosis is low. Transabdominal ultrasonography is an effective method for detecting peptic ulcer in low-weight children^[20]. Therefore, sonographers should carefully evaluate indirect findings around the stomach or duodenum^[21]. Fifteen cases were diagnosed by gastrointestinal CEUS,

the diagnostic accuracy was 88.2% (15/17), and the coincidence rate was 95.3% (41/43). Ultrasound showed that the shape of the duodenal bulb was irregular, the area was small, the local intestinal wall showed hypoechoic thickening, the mucosal folds of the duodenal wall were thickened, the ulcer surface had local depression, and strong echo spots could be seen on the surface. Gastrointestinal CEUS missed diagnosis in two cases, which may be because the ulcer area was smaller, and the gastric and duodenal ulcer in children is more difficult to see than in adults^[22]. The lesion is small, with a diameter of 3–4 mm, and the ulcer is superficial, the bottom is smooth, and the thickening of the gastric wall around the ulcer is not obvious, so it is easy to miss diagnosis. The occurrence of these missed cases shows the limitations of CEUS. It is less sensitive to small and superficial upper digestive tract ulcers and requires a high level of operator skill. However, compared with gastroscopy, CEUS has advantages in compliance, repeatability, incidence of complications and tolerance in children.

Our study had some limitations. Only a few cases were selected. Only the examination results and coincidence rate were analyzed, and the correlation between the size, location, age, weight and diagnostic accuracy of ulcer was not studied in depth. The children with peptic ulcer were not re-examined to evaluate the clinical treatment effect and supervise the recurrence.

RESULTS

Seventeen cases (15 male, 2 female) of peptic ulcer were diagnosed by gastroscopy. Fifteen children were positive for *Helicobacter pylori* antibody and had different degrees of abdominal pain. Hemoglobin decreased by varying degrees in laboratory examination. Hemoglobin level was 51–105 g/L, with an average of 82.1 ± 13.8 g/L. There were also 26 cases of nonpeptic ulcer.

Routine ultrasound diagnosed eight cases of peptic ulcer, 35 cases of nonpeptic ulcer and there was nine missed diagnoses. The results are compared with gastroscopy in Table 1.

Gastrointestinal CEUS diagnosed 15 cases of peptic ulcer, 28 cases of nonpeptic ulcer, and there were two missed diagnoses. The results are compared with gastroscopy in Table 2.

DISCUSSION

General information

We investigated 43 children with gastrointestinal symptoms in our hospital from January 2021 to June 2022. All patients were examined by routine ultrasound, gastrointestinal CEUS, and gastroscopy. Eight patients (all male) with peptic ulcer were diagnosed by routine ultrasound, The age was 8–15 years, with an average of 10.8 ± 2.5 years. Fifteen patients (13 male, 2 female) with peptic ulcer were diagnosed by gastrointestinal CEUS. The age was 8–15 years, with an average of 11.4 ± 2.3 years. The above cases all had different degrees of upper gastrointestinal symptoms, such as epigastric fullness, nausea, vomiting, and epigastric pain. Some children showed periodic epigastric pain, empty abdominal pain or nocturnal pain, intermittent black stools, and anemia. The above children were compared with those who were examined by gastroscopy.

Gastroscopy

The gastroscopy method was based on the consensus of experts on gastroscopy and colonoscopy for children in Europe [4].

Routine ultrasound

Color Doppler ultrasound was performed using a Philips EPIQ7 color Doppler ultrasound diagnostic instrument (Philips, Netherlands), L12-5 Linear array probe, at a frequency of 5–12 MHz. The patients ate a light diet the day before the inspection, and avoided food that can produce gas and is not easy to digest. Patients fasted for 8 h and refrained from drinking for > 4 h before examination. Contrast agent produced by Huqingtang (Hangzhou, China) was chosen. Before taking the contrast agent, the

contraindications such as gastrointestinal perforation, acute gastric dilatation and intestinal obstruction were eliminated by whole abdominal scan. The contrast agent was added to 150–200 mL water at 35–45°C, stirred well, and hot water at > 90°C was added to make 400–500 mL. This was stirred again and set aside. After cooling to a suitable temperature, the patient took the fluid orally. The dose depended on the age of the child: 3–10 years, 200–400 mL; 10–15 years, 400–500 mL.

CEUS

CEUS was performed by the same ultrasound physician on the same machine, and they did not know the pathological results of the child before the examination. Mainly in sitting, supine and right supine positions, a series of vertical and transverse and oblique scans were performed in the left middle and upper abdomen. There were the following scanning sections. (1) Cardia and lower esophagus (Figure 1A). The probe was placed obliquely under the left costal region near the xiphoid process and rotated to the left and rear to obtain the long-axis sonogram of the lower esophagus and cardia, and then the cross-exchange scan was performed to obtain the short-axis section and sonogram of the cardia and lower esophagus. (2) Gastric fundus (Figure 1B). The probe was tilted to the left quarter rib and rotated to the left, posterior and upper, with an angle range of 0–80°. This section showed the fundus sonogram more completely. (3) Gastric body (Figure 1C). The long axis of the gastric body can be displayed when the probe is positioned longitudinally on the left upper abdomen, and the short axis of the gastric body can be displayed when the probe is moved horizontally on the left upper abdomen. (4) Gastric angle (Figure 1D). The probe was placed horizontally on the abdomen and scanned continuously around the umbilical cord to obtain a sonogram similar to the “double ring sign”. The double-ring junction was the cross section of the gastric angle, the left ring was the gastric body, and the right ring was the gastric antrum. (5) Gastric antrum (Figure 1E). The long axis of the probe was placed obliquely between the navel and the right upper abdomen, and the longest acoustic image of the gastric cavity was obtained by scanning at different angles. Moving left and right or up

and down in this direction, yielded a complete image of the long axis of the gastric antrum. By positioning the probe in the long axis section of the gastric antrum, the complete short axis image of the gastric antrum was obtained by continuous cross scanning. (6) Gastric coronal oblique section (Figure 1F). The probe was placed obliquely between the periumbilical region and the left upper abdomen, and a continuous lateral scan to the right front showed a clear gastric coronal oblique section. (7) Duodenum (Figure 1G). The probe was longitudinally placed in the right upper abdomen, its upper end rotated 60° to the right and 30° to the left, and the lower end of the probe was relatively fixed. A more complete duodenal sonogram was obtained in this range. We observed the duodenal bulb, and the descending, horizontal and ascending duodenum.

Typical CEUS findings of peptic ulcer

We observed local thickening of the gastric wall, and interruption and depression of the gastric mucosa at the bottom of the ulcer. The diameter of the ulcer was 5–10 mm, the shape was fairly regular, the edge was symmetrical and slightly raised, and it had a crater-like appearance. The thickened gastric wall at the base of the depression and around it showed low echo. The concave surface of the mucous membrane was flat. Peptic ulcer showed speckled hyperecho under contrast-enhanced ultrasonography. The local peristalsis of the gastric wall was weakened or disappeared. Duodenal bulbar ulcer showed localized thickening of the intestinal wall, deformed bulb, poor fluid filling, localized depression on the surface of duodenal bulbar ulcer with a diameter of - 10 mm, and strong echo spots on the surface.

3 *Statistical analysis*

SPSS version 16.0 was used for statistical analysis. The numerical data (diagnostic results, coincidence rate, and diagnostic accuracy) were tested by χ^2 test and expressed as percentages. $P < 0.05$ indicated a significant difference.

CONCLUSION

Diseases of the digestive system are common in childhood, and peptic ulcer is also common in clinical practice. However, the clinical symptoms of peptic ulcer in children are not typical and there is a lack of specific symptoms and signs in the early stage. Children cannot accurately express conscious symptoms or it is difficult to accurately describe the location and nature of the symptoms, resulting in missed diagnosis or misdiagnosis of peptic ulcer. Gastroscopy can directly observe the gastric and duodenal mucosa and the degree of pathological changes, which is the gold standard for diagnosis of gastrointestinal diseases^[1]. However, as gastroscopy is an invasive method, clinicians and parents have some concerns about whether children can tolerate the examination process, and its safety^[2]. At present, with the improvement of ultrasonic image resolution and the continuous improvement and development of ultrasonic diagnostic technology, contrast-enhanced ultrasonography (CEUS) is safe, simple and noninvasive, which makes the acceptance of patients higher^[3].

This was a analysis of 43 children with digestive tract symptoms treated in our hospital from January 2021 to June 2022, to explore the clinical diagnostic value of routine ultrasound and gastrointestinal CEUS in children with peptic ulcer.

ARTICLE HIGHLIGHTS

Research background

In a larger study, we will investigate the correlation between the size, location, age, weight and diagnostic accuracy of ulcers, and re-examine the children with peptic ulcer after regular treatment by gastrointestinal CEUS.

Research motivation

CEUS has advantages in compliance, repeatability, incidence of complications, and tolerance of children, and has a high coincidence rate for clinical diagnosis. it can be used as a preliminary screening method for children with epigastric pain and an effective supplement to gastroscopy.

Research objectives

This study found that the diagnostic coincidence rate of conventional ultrasound was lower than that of gastrointestinal CEUS, and the results of gastrointestinal CEUS and gastroscopy were highly consistent, which confirmed that gastrointestinal CEUS had some advantages. The research on gastrointestinal CEUS in children was supplemented and improved. At present, gastrointestinal CEUS is not widely used in children, and it is necessary to establish the norms and standards of CEUS examination in children, which is helpful to better guide ultrasound physicians to carry out examination and improve the accuracy of examination.

Research methods

The contrast agents used in CEUS examination are food-grade contrast agents, which are safe, with no adverse effects or smell, and easy to drink. The contrast medium is a little sweet, easy for children to accept, and there is no need for intravenous sedative or general anesthesia. The examination process is painless, greatly reducing the anxiety of children and their families. ¹ The sound velocity and impedance of the contrast medium are similar to those of the liver. After oral administration of the contrast medium, the stomach and duodenum show uniform, medium and high dotted echoes, and at the same time, the gastric emptying time is prolonged. Under the gastrointestinal transmission window, the gastrointestinal wall structure and its pathological changes can be displayed more clearly. CEUS can also observe gastric peristalsis and extragastric tissue, and improve the diagnosis of gastroduodenal diseases.

Research results

The main goal of this study was to find the most suitable preliminary screening method for the diagnosis of peptic ulcer in children. For children who have contraindications for gastroscopy, CEUS can be a new option. For children with recurrent abdominal pain and other upper gastrointestinal symptoms with unknown etiology, gastrointestinal CEUS can provide a reference for clinical selection of appropriate treatment. For

children with peptic ulcer who have been diagnosed and received regular drug treatment, the curative effect can be observed and evaluated repeatedly.

Research conclusions

The common examination methods for upper gastrointestinal ulcer in children include upper gastrointestinal X-ray barium meal examination, gastroscopy, gastric computed tomography, and gastric CEUS. In children, it is particularly important to find a simple, noninvasive examination method. CEUS is simple and noninvasive, the examination process is not painful, and there is no need for sedation or anesthesia, especially for children. It is expected to become a routine examination method for the diagnosis of digestive diseases in children.

Research perspectives

The detection rate of peptic ulcer in children is increasing, with developments in diagnostic procedures. Most children show abdominal pain, but cannot accurately describe it, so it is easy to miss diagnosis, misdiagnose, and delay treatment. Gastroscopy is the gold standard for the diagnosis of peptic ulcer, but it is an invasive examination. To maximize the diagnostic efficiency and reduce the risk, gastrointestinal contrast-enhanced ultrasound (CEUS) screening is feasible before gastroscopy as an effective supplement to gastroscopy.

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ORIGINALITY REPORT

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