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Serum substance P and vasoactive intestinal peptide levels in infants with acute intussusception

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Abstract

Objective: We aimed to investigate the role of the intestinal neurotransmitters vasoactive intestinal peptide (VIP) and substance P (SP) at different time points in infants with acute intussusception.

Methods: Thirty patients who were diagnosed with acute intussusception were enrolled in the study and classified as the experimental group. Another 30 patients with an indirect inguinal hernia who had no intestinal injury were included as the control group. Serum SP and VIP levels at different time points, including pre- and postoperation, were detected by enzyme-linked immunosorbent assay and compared between the two groups.

Results: Serum SP levels in patients with acute intussusception were significantly higher than those in controls. However, with recovery of acute intussusception, SP levels gradually decreased after treatment. Serum VIP levels in patients with acute intussusception were significantly lower than those in controls. However, with recovery of acute intussusception, VIP levels gradually increased after treatment.

Conclusions: SP and VIP levels may have a potential relationship with the pathogenetic process of intussusception.

Keywords

Intussusception, enteric nervous system, substance P, vasoactive intestinal peptide, inguinal hernia, infant, bowel

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Introduction

Acute intussusception is a common acute abdominal disease in infants, while most cases in early childhood are idiopathic. Acute intussusception occurs when one segment of the bowel telescopes into an adjacent part of the bowel. If this condition uncontrolled, it may lead to intestinal necrosis and perforation.[1]

Normally, intestinal peristalsis relies on integrative action of the enteric nervous system (ENS), interstitial cells of Cajal, and intestinal smooth muscle. The ENS plays a major role that controls multiple gut function, including motility, blood flow, secretion, immunological reactions, and inflammatory reactions. There is discrete evidence that abnormalities within this network may contribute to the pathophysiological basis of some forms of idiopathic constipation.[2,3]

Substance P (SP) and vasoactive intestinal peptide (VIP) are important neurotransmitters that modulate intestinal peristalsis. SP is a major first responder to noxious or extreme stimuli. SP is rapidly released in the presence of a stressor, and induces electrical activity and mechanical contraction, which act as a stimulating peristaltic effect on the bowel.[4] VIP induces intestinal smooth muscle relaxation and plays a role in neural modulation of secretion of the pancreas and intestine.[5] SP and VIP participate in intestinal disease, such as intestinal ileus, Hirschsprung's disease, and inflammatory bowel disease.[6,7]

Neurotransmitters participate in bowel movement. However, whether there is a change in VIP and SP levels in acute intussusception remains unknown. In this study, we aimed to study the role of VIP and SP levels in acute intussusception.

Methods

Study design

This was a retrospective study of patients who received acute intussusception and were treated from December 2016 to December 2017 at Wuhan Children's Hospital. The study complied with the Declaration of Helsinki and was approved by the Review Board of Ethics Committee at Wuhan Children's Hospital (Number: WCH-20170286). During hospitalization, the children's caregivers were informed about the study and they provided written consent.

A total of 30 patients were diagnosed with acute intussusception, including 18 boys and 12 girls aged from 6 months to 3 years. All patients had typical clinical symptoms and were diagnosed by air enema or surgery. Patients who had symptoms for less than 48 hours and a relatively normal general condition underwent an air enema under X-ray. However, for those who had serious intestinal symptoms, with abdominal distension and peritonitis, or those younger than 3 months, surgical exploration was chosen. Another 30 patients with an indirect inguinal hernia who had no intestinal injury were included as the control group. The control group included 20 boys and 10 girls aged from 8 months to 2 years.

Enzyme-linked immunosorbent assay of blood samples

Blood samples (4 mL) of patients with acute intussusception were collected at 1, 2, and 4 weeks pre- and post-treatment. For some patients, we collected samples from the Inspection Department, and for other patients, we collected samples immediately after their treatment. We excluded patients

with missing samples during the time course of the study. Blood samples were immediately injected into heparin containers that included 2000 KIU antipeptidase (aprotinin; Cas 9087-70-1; Shanghai ZiYi Reagent Factory, Shanghai, China). Samples were then centrifuged at $250 \times g$ for 8 minutes at 4°C. The supernatant serum was stored at −20°C for later use. The same methods were used for sample collection in the control group.

Serum SP and VIP levels were analyzed by an enzyme-linked immunosorbent assay kit (R&D Systems, Inc., Minneapolis, MN, USA) according to the manufacturer's instructions. The absorbance (optical density value) of each sample was measured by the wavelength of 450 nm with an automatic microplate reader (Thermo Fisher Scientific, Rockford, IL, USA). A standard curve was drawn according to the standard concentrations and sample concentrations were calculated according to the optical density value.

Statistical analyses

The data are presented as the mean ± standard deviation (SD). Analysis of variance and Graph Pad Prism, version 5.0 software (Graph Pad Prism, Inc., San Diego, CA, USA) were used to determine statistical differences. P values < 0.05 were considered statistically significant.

Results

Patients' clinical characteristics

The mean age was not significantly different between patients in the acute intussusception group and those in the control group. The mean weight was also not significantly different between the two groups. Of the 30 patients with acute intussusception, three underwent an operation, including two boys and one girl. The other 27 patients were cured according to an air enema, including 16 boys and 11 girls. No patients had any complications or recurrence (Table 1).

Serum SP levels in acute intussusception

Before treatment, serum SP levels in the acute intussusception group were significantly higher than those in the control group ($P < 0.0001$) However, when patients in the acute intussusception group received surgery, serum SP levels gradually decreased ($P < 0.01$ for all time points) (Figure 1a). Patients who had a successful air enema showed the same pattern in SP levels as those who received surgery (Figure 1b).

Serum VIP levels in acute intussusception

Before treatment, mean serum VIP levels in the acute intussusception group were significantly lower than those in the control group ($P < 0.0001$), but they gradually increased after treatment ($P < 0.01$ for all

Table 1. Clinical characteristics of patients in the acute intussusception group and those of patients in the control group.

Variable	Acute intussusception group	Control group	*P* value
Mean age (y)	1.2 ± 0.6	1.3 ± 0.5	>0.05
Sex			
Male	18	20	>0.05
Female	12	10	
Mean weight (kg)	10.3 ± 0.6	11.0 ± 0.5	>0.05
Open operation			
Male	2		
Female	1		
Air enema			
Male	16		
Female	11		

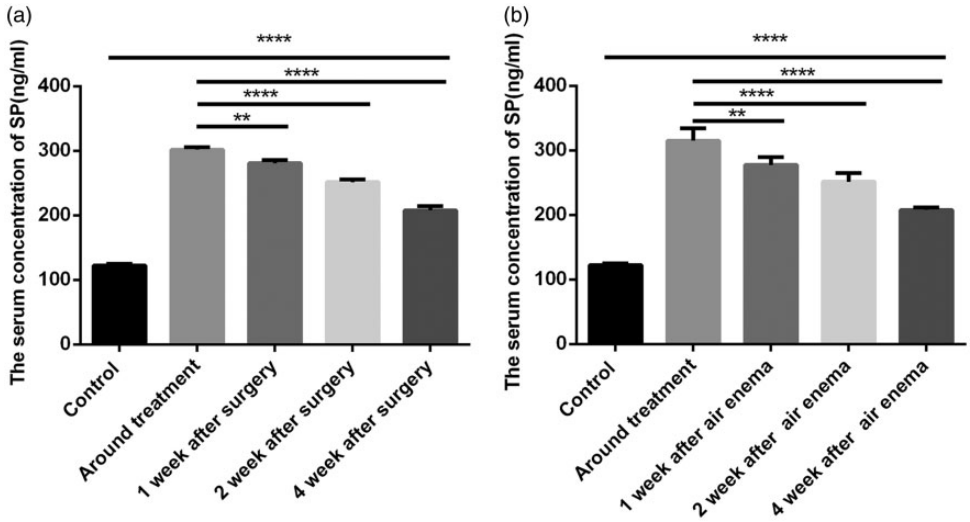

Figure 1. (a) Serum SP levels between patients with acute intussusception with surgical treatment and controls. (b) Serum SP levels between patients with acute intussusception with air enema treatment and controls. $^{**}P < 0.01$, $^{***}P < 0.001$, $^{****}P < 0.0001$. SP: substance P.

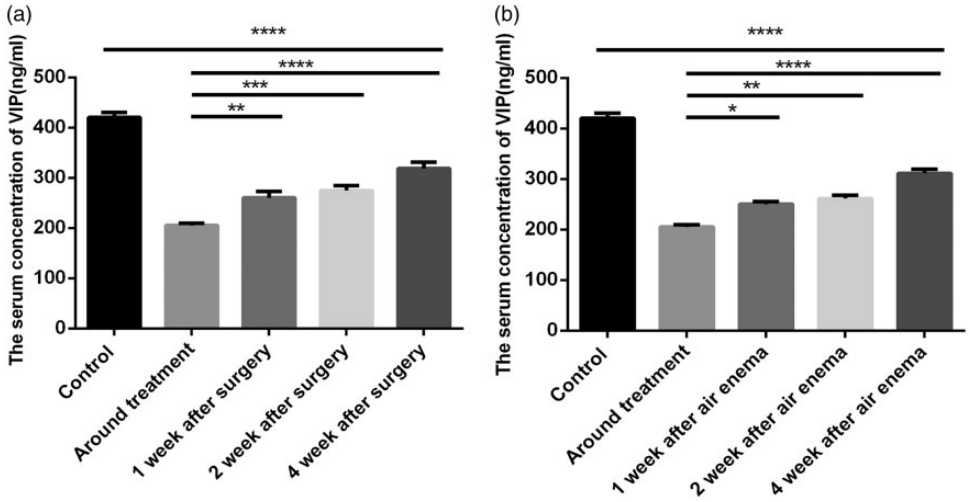

Figure 2. (a) Serum VIP levels between patients with acute intussusception with surgical treatment and controls. (b) Serum VIP levels between patients with acute intussusception with air enema treatment and controls. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$, $^{****}P < 0.0001$. VIP: vasoactive intestinal peptide.

time points) (Figure 2a). Patients who had a successful air enema showed a similar pattern of VIP expression patients who received surgery (Figure 2b).

Discussion

Intussusception occurs when one part of the intestine telescopes into another segment. Most intussusception is idiopathic and is

regarded as secondary lesions of lymphoid hyperplasia or uncoordinated bowel movement. Neurotransmitters play an important role in modulating intestinal peristalsis. In this study, we found that increased SP levels and decreased VIP levels may be related to acute intussusception in infants.

Barium saline or gas enemas are the major diagnosis and treatment methods for intussusception. However, 10% to 30% of these patients require surgical intervention. Symptoms including perforation, shock, or peritonitis provide the main indications for surgery. However, less than 25% of patients with intussusception show those signs.[1,8]

The digestive system is a special self-controlled organ that has its own ENS. The ENS is a complex system that incorporates digestion, motility, secretion, and inflammation, which function together.[9] Similar to the central nervous system, ENS neurons secrete most of the neurotransmitters, including VIP and SP. VIP is an inhibitory nonadrenergic noncholinergic neurotransmitter in the ENS. However, SP is an excitatory neurotransmitter.[9] After SP is combined with its receptors, it increases intestinal sensitivity and exerts a strong stimulus to affect intestinal smooth muscle cells. SP can induce secretion of mucus and increase vascular permeability of the bowel.[10] A previous study showed that SP can target neurokinin type 1 receptors, which directly leads to intestinal contraction in rabbits.[11] However, VIP is an inhibitory neurotransmitter that can inhibit bowel movement, relax intestinal smooth muscle, increase vasodilation, and release hormones and enzymes.[12]

A previous study indicated that neurotransmitters were altered in bowel disease.[13] This previous study showed that VIP and SP levels were increased in the colon of patients with irritable bowel syndrome. VIP levels are increased in some gastrointestinal disorders, but not in all of them.[14] Neurotransmitter levels in the blood serum can also reflect the condition of the disease. Serum and intestinal SP and VIP secretion are altered in irritable bowel syndrome.[15] SP and VIP are mainly secreted in local tissues and only a small quantity is released into the blood. However, these neurohormones in the blood serum are important indicators for predicting progress of disease. In this study, we found that SP levels were increased and VIP levels were decreased in patients with acute intussusception. This is because intussusception was caused by an intestinal motility disorder and intestinal peristalsis was accelerated during the process of intussusception. Therefore, excitatory neurotransmitters, such as SP, were increased, while inhibitory neurotransmitters were decreased after treatment. However, when the patients experienced recovery, the pathological condition was removed. Therefore, SP levels gradually decreased after an operation or air enema, while VIP levels gradually increased, which indicated that bowel movement had accelerated and recovered. These results suggest that neurotransmitter secretion is related to bowel peristalsis, and that pathological changes disturb its balance, while recovery from this disease promotes intestinal homeostasis.

In conclusion, our study shows that imbalance of intestinal excitatory and inhibitory neurotransmitters in acute intussusception, such as SP and VIP, might have a relationship with the pathogenetic process of intussusception.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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