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Relationship between childhood asthma and *Helicobacter pylori* infection

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ABSTRACT

Objective: To investigate the correlation between childhood asthma and *Helicobacter pylori* infection. **Methods:** A total of 80 children with asthma who were treated in our hospital from May 2012 to May 2015 were selected as the research subjects, and 40 cases of healthy children were selected as control group, the *Helicobacter pylori* infection of the two groups of patients were compared, the double antibody sandwich enzyme-linked immunosorbent assay was used to detect the serum *Helicobacter pylori*-IgG, *Helicobacter pylori*-CagAIgG, IL-4, *Helicobacter pylori*, IFN- γ and IL-1 β , *etc*., and the correlation between *Helicobacter pylori* infection and asthma was analyzed. **Results:** The positive rates of *Helicobacter pylori* infection in asthma group and children in attack stage were significantly higher than those in control group and children in remission stage (P<0.05). The positive rates of serum *Helicobacter pylori*-IgG and *Helicobacter pylori*-CagAIgG in asthma group and children in attack stage were significantly lower than those in control group and children in remission stage (P<0.05). The serum levels of IFN- γ in asthma group and children in attack stage were significantly lower than those in control group and children in remission stage, IL-4 and IL-1 β levels in the former were significantly higher than those in the latter (P<0.05). *Helicobacter pylori* infection positive had significant positive correlation with IL-1 β concentration (r=0.75, P<0.05). **Conclusions:** *Helicobacter pylori* infection in children has significant positive correlation with the incidence of asthma, suggesting that *Helicobacter pylori* infection has a certain protective effect on childhood asthma, but persistent *Helicobacter pylori* infection in children with asthma can aggravate the immune disorder, which is the main reason for the difficulty of treatment of asthma.

1. Introduction

Bronchial asthma is a common clinical chronic respiratory disease that mostly occurs in children, the nature of the disease is nonspecific inflammation, and the specific pathogenic mechanism is not fully clear[1]. In recent years, with the development of the society and the aggravation of environmental pollution, the morbidity and mortality of asthma in children show significantly increasing trend, causing serious effects on children's growth and health[2]. Related research[3] has confirmed that the occurrence of childhood asthma is closely related to viral infection, and respiratory syncytial virus, mycoplasma and so on are the clear pathogenic viruses for childhood asthma. *Helicobacter pylori* (*H. pylori*) is a kind of gram-negative bacilli, nearly half of the people around the world have been infected, it has correlation with the gastric ulcer, chronic gastritis and gastric cancer, *etc*., and in recent years, a number of studies have confirmed that the pathogenesis of childhood asthma is associated with *H. pylori* infection[4]. In the research, controlled study was conducted between children with asthma treated in our hospital and healthy children, and the correlation between asthma and *H. pylori* was explored to provide theoretical basis for the diagnosis and treatment of clinical childhood asthma, hereby reported as follows.

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2. Materials and methods

2.1. General information

A total of 80 children with asthma treated between May 2012 to May 2015 were selected as the research subjects, including 40 male cases and 40 female cases; they were 6-14 years old, and the average age was (11.0±3.2); BMI was 18.3-24.9 kg/m^2, and the average was (22.9±3.3) kg/m^2; 50 cases of asthma children were in attack stage, and 30 cases were in remission stage. Patients who took immunosuppressive therapy within two weeks, those whose immediate relatives had *H. pylori* infection, those with oppression in chest, anhelation, coughing and wheezing caused by other diseases and those with other diseases associated with *H. pylori* infection were ruled out. 40 cases of healthy children during the same period were selected as the control group, including 25 male cases and 15 female cases; they were 6-15 years old, and the average age was (11.8±3.7); BMI was 18.9-25.3 kg/m^2, and the average was (22.8±3.4) kg/m^2. Two groups were without significant difference in age, gender, BMI and other aspects (P<0.05), and they were comparable.

2.2. Diagnostic criteria

Diagnostic criteria for childhood asthma were as follows: (1) there were recurrent anhelation, wheezing, oppression in chest, coughing and other symptoms in children, which were mostly associated with exposure to allergens, chemical or physical stimulus, intrusion of cold air and respiratory virus infection, *etc*; (2) the onset might be accompanied by double lung audible and diffuse or scattered respiratory phase-based wheezing sound and breath phase extension; (3) bronchodilators therapy effect was remarkable.

2.3. Staging criteria for childhood asthma

(1)Acute attack stage referred to that the children were with sudden anhelation, oppression in chest, wheezing and coughing, or those with chronic inflammation showed sharp decline of FEV1 and PEF, and serious cases might show hypoxemia and carbon dioxide retention, *etc*. (2) Remission stage referred to that the children's symptoms and signs of asthma disappeared, FEV1 or PEF 80% of expected value, and maintained for 4 weeks.

2.4. Methods

2.4.1. Sampling

A total of 3 mL fasting venous blood was collected from children, let stand at room temperature for 0.5 h and centrifuged in centrifuge with 5 000 r/min for 10 min, and supernatant fluid was collected, separated and then saved in -20 ℃ condition.

2.4.2. H. pylori detection

14C urea breath testing (14C-UBT) assay was used, and *H. pylori* detector was used for tests. Before tests, children took an urea 14C capsule on an empty stomach and sat still for 30 min before tests by *H. pylori* detector, children blew into a dedicated small bottle that contained red indicator for 3 min for the first time, scintillation liquid was added after red indicator disappeared, the second blow was conducted for 3 min, *H. pylori* detector was used for detection for 2 min, 14C content in the gas was recorded, and *H. pylori* infection in children could be determined. Determination standard for 14C–UBT results: 100 dmp/(mmol•CO_2) meant (-); 100-200 dmp/(mmol•CO_2) meant (+); 200-500 dmp/(mmol•CO_2) meant (++); ＞500 dmp/(mmol•CO_2) meant (+++).

2.4.3. Detection of immune proteins and serum inflammatory factors

Double antibody sandwich enzyme-linked immunosorbent assay was used to detect the serum *H. pylori*-IgG, *H. pylori*-cytotoxin-associated gene-A (CagA)AIgG, IL-4, *H. pylori*, IFN-γ, IL-1β and other indexes, which was conducted in strict accordance with the instructions.

2.5. Statistical processing

SPSS19.0 was used to analyze data, measurement data was in terms of mean ± standard deviation (mean±sd) and were analyzed by t test, count data was by χ^2 test. P<0.05 indicated statistical significant differences.

Table 1
Comparison of *H. pylori* positive rates among included children (n, %).

Groups	Case No.	*H. pylori* negative	*H. pylori* positive	*H. pylori* positive rate
Control group	40	33	7	17.50
Asthma group	80	53	27	33.75$^{\triangle}$
Attack stage	50	25	25	50.00
Remission stage	30	28	2	7.14

Note: Compared with control group, $^{\triangle}P$<0.05; compared with remission stage, P<0.05.

3. Results

3.1. Comparison of H. pylori positive rates among included children

The positive rates of *H. pylori* infection in asthma group and children in attack stage were significantly higher than those in control group and children in remission stage, and the difference was statistically significant ($P<0.05$) (Table 1).

3.2. Comparison of serum H. pylori–IgG and H. pylori–CagA IgG expression among included children

The positive rates of serum *H. pylori*-IgG and *H. pylori*-CagAIgG in asthma group and children in attack stage were significantly lower than those in control group and children in remission stage, and the difference was statistically significant ($P<0.05$) (Table 2).

Table 2

Comparison of serum *H. pylori*-IgG and *H. pylori*-CagA IgG expression among included children (*n*, %).

Groups	No.	*H. pylori*–IgG positive	*H. pylori*–CagA IgG positive
Control group	40	25 (62.5)	19 (47.5)
Asthma group	80	30 (37.5)$^{\triangle}$	15 (18.8)$^{\triangle}$
Attack stage	50	14 (28.0)	6 (12.0)
Remission stage	30	16 (53.3)	9 (30.0)

Note: Compared with control group, $^{\triangle}P<0.05$; compared with remission stage, $P<0.05$.

3.3. Comparison of serum IFN–γ, IL–4 and IL–1β levels among included children

The serum levels of IFN-γ in asthma group and children in attack stage were significantly lower than those in control group and children in remission stage, IL-4 and IL-1β levels in the former were significantly higher than those in the latter, and the difference was statistically significant ($P<0.05$) (Table 3).

Table 3

Comparison of serum IFN-γ, IL-4 and IL-1β levels among included children (mean±sd).

Groups	Case No.	IFN-γ (pg/mL)	IL-4 (pg/mL)	IL-1β (ng/mL)
Control group	40	19.8±7.9	12.3±2.9	0.7±0.1
Asthma group	80	14.5±6.8$^{\triangle}$	24.5±4.8$^{\triangle}$	3.4±0.1$^{\triangle}$
Attack stage	50	12.2±6.9	26.2±4.7	4.5±0.1
Remission stage	30	17.9±6.6	19.8±3.4	2.1±0.1

Note: Compared with control group, $^{\triangle}P<0.05$; compared with remission stage, $P<0.05$.

3.4. Correlation analysis between H. pylori infection and serum IL–1β level among included children

IL-1β level in *H. pylori* infection positive group was significantly higher than that in negative group [(5.80±0.06) ng/mL *vs.* (0.61±0.05) ng/mL], *ie*. the *H. pylori* infection positive had significant positive correlation with IL-1β concentration ($r=0.75$, $P<0.05$).

4. Discussion

In recent years, with the development of social economy and the aggravation of environmental pollution, the incidence of bronchial asthma in children shows obvious rising trend, which causes serious impact on children's health and quality of life. Bronchial asthma is a common chronic airway mucosa inflammatory lesion, and patients are often accompanied by increased airway secretions, smooth muscle spasm and contraction[5]. Study[6] has reported that asthma onset is related to patients' nerve, endocrine, immunity, inheritance and other factors, and immune abnormality is the main cause of childhood asthma onset, and is caused by the Th1/Th2 imbalance immune system in the TC subgroup helper T cells. Thl cells are a class of pro-inflammatory cells, and the IFN-γ secreted by the cells can cause related inflammation and increase cellular immune response, thus inducing chronic airway inflammation[7]. IL-1 is a kind of lymphocyte stimulator that can stimulate T cell activation and play immunoregulatory function through the co-stimulating effect on antigen-presenting cell, its main active factor is mediated by IL-1β, and studies have confirmed that IL-1β levels significantly increase in patients with gastritis and asthma[8,9].

H. pylori is a kind of gram-negative bacteria that can proliferate in acid gastric mucosa environment and produce urease, cytokines, cytotoxin and so on to be pathogenic, and CagA plays a main role, and can induce IL-1, IL-8, INF- and other cytokines to cause serious digestive tract ulcer and incidence of tumor[10,11]. Studies[12,13] have confirmed that CagA-positive *H. pylori* strain infection can promote gastric mucosa to produce more inflammatory factors, and activate mononuclear and polymers mononuclear cells to release a series of reactive oxygen metabolites and proteolytic enzymes, thus increasing tissue injury. "Hygiene hypothesis" theory puts forward that early childhood *H. pylori* infection can stimulate Th1-related inflammatory immune response, and have protective effect on asthma onset[14], and in this study, the positive rates of *H. pylori* infection in asthma group and children in attack stage were significantly higher than those in control group and children in remission stage. Study[15] has confirmed that CagA-positive *H. pylori* strain infection is significantly negatively correlated with asthma incidence, and in this study, serum *H. pylori*-IgG and *H. pylori*-CagAIgG positive rates in asthma group and children in attack stage were significantly

lower than those in control group and children in remission stage, indicating that *H. pylori* infection could induce the Thl cells-based immune response. In addition, correlation analysis between *H. pylori* infection in children and serum IL-1 β level showed that *H. pylori* infection positive was significantly positively correlated with IL-1 β concentration, it further confirmed that in asthma children with *H. pylori* infection, the strains that mainly expressed CagA protein, in particular, could chang the balance of Thl/Th2 cells so as to ultimately protect the onset of asthma, but for the children with asthma, continuous *H. pylori* infection could increase the immune disorder and cause acute attack of asthma.

In conclusion, the incidence of children asthma has significant positive correlation with *H. pylori* infection, suggesting that *H. pylori* infection has a certain protective effect on childhood asthma, but persistent *H. pylori* infection in children with asthma can aggravate the immune disorder, which is the main reason for the difficulty of treatment of asthma.

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