Upper airway cough syndrome in 103 children

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Abstract
Background: In China, upper airway cough syndrome (UACS) is only less frequent than cough-variant asthma and accounts for 24.71% of chronic cough. This study aimed to determine the pathogenetic constituents and factors affecting UACS in children of different age groups, and to identify clinical clues for diagnosing UACS and a method for curative effect evaluation.

Methods: A total of 103 children with UACS whose chief complaint was chronic cough were studied from January to November 2013 at Children’s Hospital, Capital Institute of Pediatrics. According to their age, children with UACS were divided into 3 groups: nursing children, pre-school children, and school-age children. We analyzed the differences in pathogenetic constituents and factors affecting UACS in children. The effect of UACS treatment was evaluated by the visual analog scale (VAS) and an objective examination. Chi-squared test and analysis of variance were performed with the SPSS 19.0 statistical software.

Results: There was a high incidence of UACS in school-age children. Rhinitis with adenoid hypertrophy was the main cause of 103 suspected UACS cases. Adenoidal hypertrophy was the major cause of UACS in the pre-school children group, while rhinitis was the major reason in the nursing children and school-age children groups. Among the 103 children, there were 45 allergen-positive children, with no significant difference among different age groups. VAS scores in the different disease groups after treatment were lower than those before treatment (all \( P < 0.01 \)). VAS scores in different disease groups showed significant differences, except for 12 vs. 24 weeks after treatment \( (P=0.023) \). Different age groups had different secondary complaints.

Conclusions: There are different pathogeneses in different UACS age groups. Clinical treatment efficacy of children with UACS can be evaluated by the VAS combined with an objective examination. We recommend that the course of treatment should be 12 weeks.

Keywords: Child; Cough; Nose diseases; Therapeutics

Introduction
Chronic cough is a common and debilitating complaint in children, representing one of the most frequent reasons for parents to seek medical advice. Although there are diverse chronic cough morbidities in different countries, upper airway cough syndrome (UACS) is a major cause of childhood chronic cough. In China, UACS is only less frequent than cough-variant asthma and accounts for 24.71% of chronic cough.

The UACS is not a type of specific disease, but a syndrome of chronic cough caused by a variety of upper airway diseases. UACS includes various types of rhinosinus diseases that can induce cough, particularly allergic or non-allergic rhinitis and sinusitis. The morbidity of UACS in children differs in different age groups and in different countries and regions, with a rate of 20% to 23% in school-age children, and 1.4% in pre-school children. This study aimed to analyze the distribution of pathogenesis, clinical features, treatment, and evaluation of cases of UACS in children of different ages. We aimed to provide a basis for treatment of UACS in children.

Methods

Ethical approval
The study was conducted in accordance with the Declaration of Helsinki and was approved by the local Ethics Committee of Peking Union Medical College Hospital (No. S-K646). Informed written consent was obtained from all patients prior to their enrollment in this study.
Patients

From January 2013 to November 2013, a total of 103 pediatric patients with chronic cough as the chief complaint were enrolled at the Department of Otorhinolaryngology, Children’s Hospital Affiliated to the Capital Institute of Pediatrics. We included 58 boys and 45 girls, whose age ranged from 2.7 to 14.6 years (8.9 ± 0.8 years). All of the children who visited a doctor initially in the respiratory clinic or asthma division were transferred to the Department of Otorhinolaryngology. They underwent an X-ray examination and lung function test to exclude lung diseases. All of the children were selected from 9620 patients who were treated by the same doctor and met the inclusion criteria of this study. All children who were diagnosed with UACS were divided into the three following groups: nursing children group (0–3 years), pre-school children group (>3 to <6 years), and school-age children group (≥6 years). Among the 103 children with UACS in the three groups, there were eight (7.8%), 45 (43.7%), and 50 (48.5%) children, respectively. This study was a retrospective review.

Inclusion criteria

UACS and adenoid hypertrophy

The following criteria were used to identify UACS in children[7]: (1) Persistent coughing was present for 4 weeks, accompanied by white foam or yellow-green purulent sputum. The coughing was characterized by morning onset or changes in body position, accompanied by nasal obstruction, runny nose, dry pharynx with foreign body sensation, and repeated clearing of the pharynx. (2) There was obvious hyperplasia of the posterior pharyngeal follicles, and sometimes there were cobble-like changes or mucous or purulent secretion. The diagnosis of adenoid hypertrophy depended on the results of fiberoptic nasopharyngoscopy. Adenoid hypertrophy was diagnosed if the volume of the adenoid was larger than two thirds of the posterior naris.

Child nasosinusitis and allergic rhinitis

The diagnosis of child nasosinusitis was determined by using Advice of Diagnosis and Treatment of Child Naso-Nasosinusitis, which was published by the Subspecialty Group of Pediatric, Society of Otorhinolaryngology Head and Neck Surgery, Chinese Medical Association, in 2012.[8] The diagnosis of child allergic rhinitis was determined by using Guidelines of Diagnosis and Treatment of Chronic Cough in Children, which was published in the Chinese Journal of Pediatrics.[9]

Exclusion criteria

The exclusion criteria were as follows[10]: acute upper airway infection (<2 weeks), acute (<2 weeks), or subacute (2–4 weeks) cough, cough related to mycoplasma, pertussis, chlamydia, the presence of an underlying cardiorespiratory condition, current or recurrent wheeze (two episodes), the presence of other obvious causes of chronic cough (eg, bronchiectasis), or other respiratory symptoms (eg, productive cough, hemoptysis, and dyspnea).

Examinations

Routine examination

All children underwent a routine examination in the Department of Otorhinolaryngology, including observation of the nasal mucosa, turbinate, nasal passages, secretion and its property in nasal passages, the nasal septum, and oropharyngeal mucosa, the degree of hypertrophy of the tonsils, and posterior pharyngeal wall mucosa.

Nasopharyngoscopy

All children underwent fiberoptic nasopharyngoscopy (Olympus, Tokyo, Japan). The degree of adenoid hypertrophy and secretion properties from nasopharyngeal reflux were examined.

Computed tomography scan

Children with sticky purulent secretion in the nasal cavity or with a headache as the chief complaint underwent a paranasal sinus computed tomography (CT) scan (Optima 660; GE, Norwalk, CT, USA).

Allergen detection

All children underwent allergen detection (allergen skin prick or serum-specific immunoglobulin E test).

Treatment

All of the children who were diagnosed with UACS were initially treated by using drugs to make it easier to compare treatment effects. The treatment included saline nasal irrigation, glucocorticoid in the nose, antihistamines, a leukotriene receptor antagonist, mucus excrict, and antibiotics (in some children with nasosinusitis). The course of treatment lasted for 12 weeks.

Evaluation of treatment

Objective evaluation included an electronic nasopharyngeal fibroscope examination 1 month after treatment and/or a paranasal sinus CT examination 3 months after treatment. We used the visual analog scale (VAS) to quantify the children’s or their parents’ feelings toward a change of symptoms before and after treatment. We adopted the linear scoring method as follows. A straight line was scaled as 0 to 10 cm in which 0 indicates no cough and 10 indicates the most serious cough. The larger the number, the more serious the cough. Patients and/or parents evaluated their own cough by themselves. We used the VAS in all 103 children in our study before treatment and at 2, 4, 8, 12, and 24 weeks after treatment.

Follow-up

All of the children were followed up by a clinic. All of the children were followed up until April 2016.

Statistical analysis

The normal distribution of count data was tested. The Chi-squared test and analysis of variance (ANOVA) were
performed using SPSS 19.0 statistical software. The Chi-
squared test was used to compare the ratio of pathogenesis
of UACS. ANOVA was used to compare the statistical
difference between two time points in different disease
groups. A statistically signi
ificant difference was considered
as $P < 0.01$.

Results

Pathogenesis of UACS

Among all the 103 UACS children, there were 22 cases
(21.4%) of rhinitis, 17 cases (16.5%) of nasosinusitis,
10 cases (9.7%) of adenoid hypertrophy, 38 cases (36.9%)
of rhinitis with adenoid hypertrophy, and 16 cases (15.5%)
of nasosinusitis with adenoid hypertrophy. There was a
significant difference in the pathogenesis of UACS among
different age groups, Pearson Chi-squared test: 27.379,
$P < 0.001$ [Table 1]. To further analyze the effect of nasal
and/or nasopharyngeal single disease on chronic cough, the
data were sorted again. There was also a significant
difference in the pathogenesis of UACS among the different
disease groups, Pearson Chi-squared test: 16.299,
$P < 0.001$ [Table 2]. Adenoid hypertrophy was the main reason for
cough in pre-school children with UACS, while it was rhinitis
in nursing children and school-age children with UACS.

Effect of allergic factors on UACS

A total of 45 children were allergic antigen positive, with
29 boys and 16 girls, the gender ratio was 1.8:1. A total of
58 children were allergic antigen negative, with 29 boys
and 29 girls. There was no significant difference in the
allergic antigen-positive rate among the different age
groups, Pearson Chi-squared test: 3.282,
$P = 0.070$ [Table 3]. This
finding indicated that an allergy was not
the main factor that caused a significant difference among
the different age groups.

Evaluation of treatment

Visual analog scale

The VAS data, including the whole course of treatment,
were regrouped by diagnosis and fit a normal distribution
($P > 0.05$), as verified by the Kolmogorov-Smirnov test.
There was no significant difference in diagnosis among the
different disease groups ($F_{\text{disease}} = 0.752$, $P_{\text{disease}} = 0.571$).
The VAS scores at different treatment times (2, 4, 12, and
24 weeks) were significantly lower than those before
treatment ($F_{\text{treatment time}} = 234.556$, all $P_{\text{treatment time}} < 0.01$). After treatment, the VAS score at different times was

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Table 1: Etiology of upper airway cough syndrome among different age groups.

| Groups            | n    | Rhinitis | Nasosinusitis | Adenoid hypertrophy | Rhinitis with adenoid hypertrophy | Nasosinusitis with adenoid hypertrophy | $\chi^2$ | P       |
|-------------------|------|----------|---------------|---------------------|----------------------------------|----------------------------------------|---------|---------|
| Nursing children group | 8    | 6 (75.0) | 0             | 2 (25.0)            | 0                                | 21.250                                 | <0.001  |
| Pre-school children group | 45   | 3 (6.7)  | 4 (8.9)       | 10 (22.2)           | 22 (48.9)                       | 6 (13.3)                               | 33.333  | <0.001  |
| School-age children group | 50   | 13 (26.0)| 13 (26.0)     | 0                   | 14 (28.0)                       | 10 (20.0)                              | 16.750  | 0.002   |
| Total             | 103  | 22 (21.4)| 17 (16.5)     | 10 (9.7)            | 38 (36.9)                       | 16 (15.5)                              | 27.379  | <0.001  |

Data are presented as $n$ (%).

Table 2: Etiology of upper airway cough syndrome among different age groups.

| Groups            | n    | Single disease in total, n | Rhinitis $^*$ | Nasosinusitis $^*$ | Adenoid hypertrophy $^*$ | $\chi^2$ | P       |
|-------------------|------|---------------------------|--------------|--------------------|------------------------|---------|---------|
| Nursing children group | 8    | 10                        | 8            | 0                  | 2                      | 15.600  | <0.001  |
| Pre-school children group | 45   | 73                        | 25 (34.2)    | 10 (13.7)          | 38 (52.1)              | 24.206  | <0.001  |
| School-age children group | 50   | 74                        | 27 (36.5)    | 23 (31.1)          | 24 (32.4)              | 0.527   | 0.768   |
| Total             | 103  | 157                       | 60 (38.2)    | 33 (21.0)          | 64 (40.8)              | 16.299  | <0.001  |

$^*$Data are presented as $n$ (%).

Table 3: Allergic factors in children with upper airway cough syndrome among different age groups.

| Groups            | n    | Positive | Negative | $\chi^2$ | P       |
|-------------------|------|----------|----------|---------|---------|
| Nursing children group | 8    | 5        | 3        | 1.000   | 0.317   |
| Pre-school children group | 45   | 17 (37.8)| 28 (62.2)| 5.378   | 0.020   |
| School-age children group | 50   | 23 (46.0)| 27 (54.0)| 0.640   | 0.424   |
| Total             | 103  | 45 (43.7)| 38 (56.3)| 3.282   | 0.070   |

Data are presented as $n$ (%).
significantly different, except for 12 vs. 24 weeks after treatment ($P=0.023$), which might indicate the endpoint of treatment [Figure 1].

**Objective evaluation**

A total of 50 children underwent a paranasal sinus CT examination, which led to 33 children being diagnosed with nasosinusitis. Three months after treatment, nasal mucosal inflammation was improved in paranasal sinus CT imaging [Figure 2].

**Secondary complaints**

Chronic cough was the chief complaint of all children with UACS in this study. The ranking of secondary complaints of children with UACS was different in the different age groups. Secondary complaints of UACS were breathing with the mouth open in six (75.0%) cases, snoring in one (12.5%) case, and rhinorrhea in one (12.5%) case in the nursing children group (eight cases in total). Secondary complaints of UACS were snoring in 23 (51.1%) cases, breathing with the mouth open in 13 (28.9%) cases, nasal obstruction in six (13.3%) cases, and rhinorrhea in three (6.7%) cases in the pre-school children group (45 cases in total). Secondary complaints of UACS were snoring in 18 (36.0%) cases, rhinorrhea in 13 (26.0%) cases, headache in nine (18.0%) cases, nasal obstruction in six (12.0%) cases, chest tightness in two (4.0%) cases, hyposmia in one (2.0%) case, and breathing with the mouth open in one (2.0%) case in the school-age children group (50 cases in total).

**Follow-up**

All of the children were followed up until April 2016. There was no constant cough persisting longer than
4 weeks. Eight children had low temperature plasma adenoid radiofrequency ablation through a nasal endoscope because of adenoid hypertrophy between 2015 and 2016.

Discussion

There is moderate quality evidence that common etiologies of chronic cough in children are different from those in adults and are dependent on age and setting.[11] UACS includes various types of rhinosinus diseases that can induce cough, particularly allergic or non-allergic rhinitis and sinusitis. Tonsillar hypertrophy, which causes tissue impingement of the epiglottis, has also been reported to cause chronic cough in children. However, the pathogenesis and mechanism of UACS are unclear.

Pathogenesis in different UACS age groups

The pathogenesis of chronic cough in children is not the same as that in adults, and differs among various age groups.[7,12] In our study, we found that rhinitis with adenoid hypertrophy was the major pathogenesis of chronic cough among 103 children with UACS. We found that children suffered from different pathogeneses in different age groups. Rhinitis was the major pathogenesis in the nursing children and school-age children groups, while it was adenoid hypertrophy in the pre-school children group. This finding clearly showed that inflammation and/or mechanical obstruction were two major causes of UACS in children. As children became older in our study, the diagnostic frequency of rhinitis and nasosinusitis markedly increased in the school-age children group compared with the pre-school children group and nursing children group. Furthermore, the diagnostic frequency of adenoid hypertrophy showed a related decrease.

As children grow, their range of activity expands, thus increasing the opportunity of contacting pathogenic microorganisms, which induces an inflammatory reaction. Because the immune system of children has not yet developed, coughing may be the result of the respiratory system serving as a part of the whole immune system. This could explain why some children with backflow do not get develop a cough, while those without backflow show the symptoms of cough.[13,14]

Allergic rhinitis is one of the most common nasal diseases which causes UACS in children.[3,15] The mechanism of continuously inhaled allergens causing coughing is relatively clear.[16] There were no significant differences in allergic factors among the different age groups, which indicated that allergic disease is an important causal factor for UACS in children of different ages. Regardless of the children’s age, anti-allergenic therapy is necessary.

Treatment time of UACS

The process of treatment for UACS in children is also a process of making a clear diagnosis. According to the American College of Chest Physicians, during the diagnosis and treatment process of non-specific chronic cough, attention should be paid to the expectation of children’s parents.[17] Furthermore, they emphasize the importance of follow-up and re-evaluation (ie, observation, waiting, and follow-up).

We found that the VAS scores were significantly different at different times before and after treatment among the different disease groups. Therefore, using standard treatment to improve UACS in children is a gradual process. Drug treatment of most children lasted approximately 12 weeks. Therefore, waiting and observation lasted from 12 to 24 weeks after treatment. This suggested that, for most children with UACS, standard drug treatment began to take effect from 2 weeks after treatment, and 12 weeks after treatment was the end of treatment.

For a long time, UACS in children was attributed to “non-specific cough” and always lacked specific clinical symptoms. Common complications (besides cough) mentioned by most studies include sneezing, rhinocnesmus, nasal obstruction, rhinorrhea, facial pain, and dysosmia. In our study, complications of UACS in children varied among different age groups. Different complications were closely related to different pathogeneses in different age groups. These findings suggest that children and parents of different age groups should pay close attention to their own symptoms. Nursing children and pre-school children lack the ability to express themselves. Therefore, the chief complaint always reflects the parents’ attention. Consequently “breathing with the mouth open” ranked first as the main complaint in our study. As children age, their own awareness and skill for expression gradually improve. Therefore, in the school-age children group in our study, “breathing with the mouth open” ranked last, and chief complaints, such as “rhinorrhea,” “ache,” “nasal obstruction,” and “chest tightness,” began to increase. Good communication and attention to feelings of children and their parents can help identify effective clues for diagnosing UACS in children.
A limitation of our study is that it was a small-sample, retrospective study. A randomized, prospective study needs to be performed in the future. Nevertheless, the conclusion of the study has certain clinical value and can guide clinicians, especially pediatricians, in diagnosis and treatment of children with UACS.

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Conflicts of interest
None.

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