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RESEARCH ARTICLE

Evaluation of chronic cough etiology, quality of life, and anxiety level in children

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ABSTRACT

Evaluation of chronic cough etiology, quality of life, and anxiety level in children

Introduction: *To evaluate the quality of life and anxiety level of school-age children with chronic cough, and changes with treatment.*

Materials and Methods: *Patients aged between 6-18 years with a chronic cough were included in this study. A control group was designed, and the scale scores were compared with each other.*

Results: *The mean age of the 82 patients was 10.9 ± 3.8 years, 62 (75.6%) had at least one specific cough marker. Forty patients (48.8%) were diagnosed with asthma. At their first visit, the psychosocial health scores and the total scale scores (sum of physical and psychosocial total scores) were lower than the control group for both patients and parents. After the resolution of cough, their scores increased to the same level with the control group. It was also found that the level of anxiety was significantly higher than in the control group both before treatment and after the resolution period (p< 0.001 and =0.008, respectively).*

Conclusion: *Asthma was the leading cause of chronic cough. Quality of life is impaired in children with chronic cough. Anxiety level in these patients increases and after symptoms improve, continues to be higher than that of healthy children.*

Key words: *Anxiety level; asthma; chronic cough; children; quality of life*

ÖZ

Çocuklarda kronik öksürük etiyolojisi, yaşam kalitesi ve kaygı düzeyinin değerlendirilmesi

Giriş: *Kronik öksürük şikayeti olan okul çağı çocuklarında yaşam kalitesi ve anksiyete düzeyleri ve tedavi ile değişiminin değerlendirilmesi.*

Materyal ve Metod: *Çalışmaya 6-18 yaş arası kronik öksürüğü olan hastalar dahil edildi. Kontrol grubu oluşturuldu ve ölçek puanları karşılaştırıldı.*

Bulgular: *Seksen iki hastanın yaş ortalaması 10,9 ± 3,8 yıldı, 62'sinde (%75,6) en az bir spesifik öksürük belirteci vardı. Kırk hastaya (%48,8) astım tanısı kondu. İlk ziyaretlerinde hem hastalar hem de ebeveynler için psikososyal sağlık puanı ve toplam ölçek puanı (fiziksel ve psikososyal toplam puan toplamı) kontrol grubundan daha düşüktü. Öksürük düzeldikten sonra puanları kontrol grubu ile aynı seviyeye yükseldi. Ayrıca, hem tedavi öncesi hem de iyileşme dönemi sonrasında kaygı düzeyinin kontrol grubuna göre anlamlı düzeyde yüksek olduğu bulundu (sırasıyla p< 0,001 ve =0,008).*

Sonuç: *Kronik öksürük şikayeti olan hastalar en sık astım tanısı almıştı. Kronik öksürüğü olan çocuklarda yaşam kalitesi bozulur. Bu hastalarda kaygı düzeyi artar ve semptomlar düzeldikten sonra sağlıklı çocuklara göre daha yüksek olmaya devam eder.*

Anahtar kelimeler: *Anksiyete düzeyi; astım; kronik öksürük; çocuklar; yaşam kalitesi*

INTRODUCTION

Chronic cough in children is defined as a cough that persists for longer than four weeks. Cough is one of the most common reasons for admission to outpatient clinics in children. Most of these children need to visit a doctor more than five times a year for medical consultation (1-3). Chronic cough in children differs from that in adults, and it should be regarded as a symptom of an underlying disease (4,5). Evaluation of chronic cough begins with a detailed history and a thorough physical examination. A chest x-ray and if possible, spirometry may help the diagnosis. When specific causes of cough are suspected, further investigations are needed. Reassuring the child and the family and removing irritants such as tobacco smoke are important, and the patient must be carefully evaluated and followed up (1,2).

When specific causes are not identified, however, the prolonged time course of coughing may result in some psychosocial issues in both the child and other family members. Caregivers are worried about underlying reasons of the cough. Parents of children with chronic cough had higher stress which caused emotional distress when their children were coughing, and when the coughing stopped, the problem returned to normal (6). It has been found that children with chronic diseases have a lower quality of life and higher anxiety level than healthy children (7,8). Patients with chronic disease may experience frequent hospitalizations, disruptions in friendships, physical limitations, poor sleep quality, and poor academic performance. As a result, children's quality of life can be impacted by chronic cough (9-12).

In this study, we aimed to evaluate the quality of life and anxiety level of school-age children with chronic cough, and changes with treatment.

MATERIALS and METHODS

Study Design

This prospective cohort study was conducted in a tertiary pediatric hospital. Patients with chronic cough (>4 weeks) who were admitted to the pediatric allergy, pediatric pulmonology and general pediatrics outpatient clinics between September 2017 and February 2018 were included in our study. Age range of patients was limited to 6-18 years and those with a previous diagnosis of chronic disease (including asthma, cystic fibrosis, immunodeficiency) were excluded. The study was approved by the local ethics committee (8.6.2017/082), and informed consent was obtained from the patients.

Clinical Protocol

Patients were evaluated according to the chronic cough guideline published by the American College of Chest Physicians (ACCP) (13). Demographic characteristics, socio-economic level, medical history, and patient complaints were recorded. A pulmonary function test (conducted by an experienced nurse) and chest radiography were performed on all patients during their first visit. Specific cough pointers (abnor-

mal pulmonary function test, presence of sputum, dyspnea, hemoptysis, heart murmur, etc.), which are outlined in the ACCP guidelines, were determined for each patient (13). Depending on the specific cough pointers, a complete blood count, immunoglobulin (Ig) G-A-M-E levels test, sweat test, skin prick test, allergen-specific IgE test, tuberculin skin test (PPD), bronchoscopy, and computed tomography (CT) scan were also performed when needed. All patients were evaluated at 2-4 week intervals thereafter.

We were unable to use a disease-specific questionnaire (e.g., a child chronic cough specific QoL questionnaire) to assess quality of life because it had not been translated and validated in our language; therefore, we chose a general health-related quality of life scale. For this purpose, the Pediatric Quality of Life Inventory (PedsQL) was used (14-16). This questionnaire consists of 23 questions that evaluate physical and psychosocial health. We obtained three scores from the answers: physical total score, psychosocial total score, and total scale score. The PedsQL was given to all patients over the age of eight, as well as their parents, during their first visit and one month after their cough had resolved. In the PedsQL, higher scores indicate a higher quality of life. The State-Trait Anxiety Inventory 1 (STAI-1) and the State-Trait Anxiety Inventory 2 (STAI-2) were used to evaluate the level of anxiety in patients over the age of eight (17,18). These tests consist of 20 questions: While STAI-1 measures how a child feels 'at this moment/state', STAI-2 measures how they feel 'in general/trait'. Both tests were performed during the first visit, but only STAI-1 was performed one month after the resolution of cough. In STAI-1 and STAI-2, higher scores indicate a higher level of anxiety. STAI-1 and STAI-2 questionnaires were filled by both patients and parents. Patients or parents who refused to fill out the questionnaires were not included.

A control group was created from patients who presented at the general pediatric outpatient clinic for routine control. They were chosen from children of similar age, gender, and socioeconomic status who had not previously been diagnosed with a chronic disease. The PedsQL, STAI-1, and STAI-2 questionnaires were given to children and parents who agreed to fill out the forms.

Statistical Analysis

The SPSS ver. 18.0 for Windows (Chicago: SPSS Inc, 2009) software was used to calculate statistical data. Continuous variables were expressed with arithmetic mean, standard deviation, median, and minimum, maximum values whereas categorical variables were expressed in numbers (n) and percent (%). The compatibility of continuous variables with normal distribution was tested with Kolmogorov-Smirnov. The Pearson chi-square and Fisher's exact tests were used in the analysis of categorical variables. The Mann-Whitney U test was used in the analysis of continuous variables. ANOVA test and Bonferroni correction were used to compare anxiety scale scores across diagnostic groups. A Spearman correlation analysis was used to find the relationship between state and trait anxiety inventory scores, quality of life questionnaire scores, and age. The significance level was accepted as $p< 0.05$.

RESULTS

The study included a total of 82 patients. There were 41 males (50%) and 41 females (50%). The mean age was 10.9 ± 3.8 years (range 6-17.9 years). Demographic characteristics of the patient and control groups are shown in Table 1. The mean cough duration was 6.3 ± 3.8 weeks (range 4-20 weeks. The exposure rate to passive smoking was 64.6% (n= 53), and five adolescents (11.6% of total adolescents) were active smokers. All patients were in school, and 43 (52.4 percent) had missed at least one day due to a cough in the previous month.

A posterior-anterior chest radiography and a pulmonary function test (PFT) were performed on all patients. Abnormalities were noticed in 20 (24.4%) chest radiographies (19 showed infiltration while one showed prominence in the pulmonary conus). The bronchodilator reversibility test was positive in 20 patients (24.4%). Other tests, such as the Ig level test, skin prick test, PPD, and sweat test, were also conducted. Of the patients, 14 (17.1%) had eosinophilia, 26 (31.7%) had high serum total IgE levels, 11 (13.4%) had positive skin prick test results, one of two sputum cultures yielded a positive result, one patient underwent bronchoscopy, and one had a thorax CT. Sweat tests were performed on eight patients and PPD on nine, with no positive results.

A total of 62 (75.6%) patients had at least one specific cough marker. The most common marker was wet cough (n= 52, 63.4%). The distribution of patients based on their specific cough markers can be seen in Table 2.

Table 1. Demographic characteristics of patient and control groups

	Total (n= 169)	Patient group (n= 82)	Control group (n= 87)	Statistics
	Median (range)	Median (range)	Median (range)	p
Age (months)	123 (72-215)	121 (72-215)	125 (72-214)	.60
	n (%)	n (%)	n (%)	p
Gender				
Female	82 (48.5)	41 (50.0)	41 (47.1)	.709
Male	87 (51.5)	41 (50.0))	46 (52.9)	
Maternal educational level				
Elementary education	76 (45.0)	35 (42.7)	41 (47.1)	.933
Secondary education	27 (16.0)	14 (17.1)	13 (14.9)	
High school	45 (26.6)	23 (28.0)	22 (25.3)	
University	21 (12.4)	10 (12.2)	11 (12.6)	
Paternal educational level				
Elementary education	63 (37.3)	30 (36.6)	33 (37.9)	.886
Secondary education	27 (16.0)	12 (14.6)	15 (17.2)	
High school	45 (26.6)	24 (29.3)	21 (24.1)	
University	34 (20.1)	16 (19.5)	18 (20.7)	
Monthly income				
<1000 TL	12 (7.1)	5 (6.1)	7 (8.0)	.907
1001-1500 TL	40 (23.7)	20 (24.4)	20 (23.0)	
1501-2500 TL	65 (38.5)	31 (37.8)	34 (39.1)	
2501-3500 TL	27 (16.0)	15 (18.3)	13.8)	
>3501 TL	25 (14.8)	11 (13.4)	14 (16.1)	

TL: Turkish liras.

Table 2. Distribution of patients with specific cough markers

	n	%
Cough markers		
Wet cough	52	63.4
Recurrent LRTI	21	25.6
Abnormal PFT	20	24.4
Fever	19	23.2
Abnormal auscultation finding	10	12.2
Effort dyspnea	9	11.0
Cardiac anomaly (including murmur)	3	3.7
Haemoptysis	3	3.7
Tuberculosis contact history	3	3.7

LRTI: Lower respiratory tract infection, PFT: Pulmonary function test.

Asthma (n= 40, 48.8%) was the most common diagnosis in patients presenting with chronic cough. At their first evaluation, 27 were diagnosed as asthmatic based on their PFT, medical history, and examination. Among the patients that had a nonspecific cough, 13 were diagnosed as asthmatic during the

follow-up period. Protracted bacterial bronchitis (PBB) was the second most common diagnosis. Of the 24 patients (29.3%) diagnosed with PBB, 22 suffered from wet cough at the first visit, while two patients had a nonspecific, dry cough that did not resolve by the next follow-up and turned into wet cough. We administered an antibiotic treatment to all patients with PBB for two weeks. Upper airway cough syndrome was confirmed in 10 patients (12.2%) by their medical histories and examination. Post-viral cough was detected in four patients (4.9%). These patients had a nonspecific cough at their first examination that resolved without any treatment. We learned from their medical history that they had an upper respiratory tract infection before the cough symptoms started. Gastroesophageal reflux disease was suspected in two patients (2.4%) and their symptoms recovered after proton pump inhibitor treatment. A thoracic CT scan revealed a bronchial tumor in a patient with pulmonary conus enlargement, and the child was subsequently operated on. Bronchoscopy revealed vocal cord dysfunction in one patient with a nonspecific cough who did not respond to inhaled corticosteroids (ICS).

In the cough group (n= 82), 76 parents (92.7%) completed the PedsQL during the pre-treatment period and 71 parents (86.6%) completed the PedsQL after the resolution of cough. While the number of children filling out the PedsQL was 52 in the pre-treatment period, it was 49 after the resolution of cough. In the control group (n= 87), all parents and 57 children filled out the PedsQL. The median score for the PedsQL filled out by the parents in the chronic cough group in the pre-treatment period was significantly lower than in the control group for all three subscales ($p< 0.001$). When the PedsQL scores of the pre-treatment period filled out by the children (n= 52) were evaluated, the median psychosocial total score (PSTS) of patients was lower than the control group ($p= 0.007$). Also, the total scale score (TSS) was lower than the control group ($p= 0.021$). Physical health total scores of patients and control group were similar ($p= 0.158$) (Table 3). The PedsQL score distributions of both children and parents following cough resolution were found to be similar to those of the control group ($p> 0.05$ for all variables).

The Pediatric Quality of Life Questionnaire scores for children and their parents in the chronic cough group during the pre-treatment period were found to be significantly lower ($p< 0.05$ for all variables) than the scores in the control group [except for child psychosocial total score (PSTS)] ($p> 0.05$). This difference disappeared after the resolution of cough. Comparisons of the PedsQL scores for the chronic cough group and control group are shown in Table 3.

In the chronic cough group (n= 82), 53 patients filled out STAI-1 and STAI-2 in the pre-treatment period

Table 3. Comparison of the quality of life questionnaire scores of the chronic cough and the control groups

QoL scores[a]	Patient (n= 82)	Control (n= 87)	p
Pre-treatment			
Parent-PTS	65.6 (15.6-100)	84.3 (43.7-100)	**<0.001**
Parent-PSTS	71.3 (26.6-100)	85 (40-100)	**<0.001**
Parent-TSS	68.4 (22.8-100)	83.6 (41.3-100)	**<0.001**
Patient-PTS	75.1 (18.7-100)	81.2 (37.5-100)	.158
Patient-PSTS	75.8 (40.0-100)	86.6 (48.3-100)	**.007**
Patient-TSS	76.6 (32.6-98.9)	83.6 (51-100)	**.021**
After resolution of cough			
Parent-PTS	81.2 (18.7-100)	84.3 (43.7-100)	.295
Parent-PSTS	83.1 (31.6-100)	85 (40-100)	.432
Parent-TSS	82.6 (30.4-100)	83.6 (41.3-100)	.334
Patient-PTS	87.5 (21.4-100)	81.2 (37.5-100)	.198
Patient-PSTS	85.8 (40-100)	86.6 (48.3-100)	.746
Patient-TSS	85.2 (34.1-100)	83.6 (51-100)	.458

[a]: Median (minimum-maximum), PTS: Physical total score, PSTS: Psychosocial total score, TSS: Total scale score.

Table 4. Comparison of the STAI-1 and STAI-2 scores with the control group

	Total	Patient	Control	Statistics	Statistics
	n= 169	n= 82	n= 87	z	p
Anxiety scores					
Pre-treatment					
STAI-1[a]	30 (24– 54)	33 (24-54)	29 (20-40)	-3.942	**<0.001**
STAI-2[a]	30 (21-50)	32 (21-50)	29 (21-48)	-3.097	**.002**
After resolution of cough					
STAI-1[a]	30 (20-47)	32 (20-47)	29 (20-40)	-2.658	**.008**

[a]: Median (minimum-maximum), STAI-1: State-trait anxiety inventory 1 scores, STAI-2: State-trait anxiety inventory 2 scores.

and 49 children filled out STAI-2 after the resolution of their cough. In the control group (n= 87), 57 children filled out both STAI-1 and STAI-2. STAI-1 scores for children with chronic cough in the pre-treatment period were significantly higher than that of the control group (33 vs. 29, respectively; z= -3.942, p< 0.001), and this situation persisted after the resolution of cough (33 vs. 29, respectively; z= 2.658, p= 0.008). Likewise, STAI-2 scores were found to be significantly higher in children with chronic cough compared to the healthy control group (32 vs. 29, respectively; z= -3.097, p= 0.002) (Table 4).

To compare these QoL and anxiety scores among patients, three etiological groups were compared: asthma (n= 40), PBB (n= 24), and upper airway cough syndrome (n= 10). There was no difference in QoL scores filled out by both parents and children (p> 0.05, with Bonferroni correction) between the three groups in the pre-treatment period and after cough resolution. Similarly, there was no difference between diagnostic groups in terms of cough anxiety scores in the pre-treatment period and after the resolution of cough (p> 0.005).

DISCUSSION

In this study, the disease etiology, quality of life, and anxiety levels of children between the ages of 6-18 years with chronic cough were evaluated. Forty patients (48.8%) had asthma; 24 patients (29.3%) had PBB. During the pre-treatment period, psychosocial health scores and total scale scores were lower than in the control group for both patients and parents. After the resolution of cough, the scores increased to the same level as those of the control group. In patients over the age of eight, who filled out an anxiety form, it was found that the level of anxiety was significantly higher than in the control group both in the pre-treatment period and after the resolution of cough.

The most common causes of chronic cough vary by nationality. According to global studies, the two most common causes are asthma and PBB in Europe; PBB and asthma in Australia; GERD and asthma in America; and asthma and tuberculosis in India (4,5,19-21). In our study 40 patients (48.8%) were diagnosed with asthma and 24 patients (29.3%) with PBB. Some rare diagnoses should be kept in mind, especially in treatment-resistant cases such as vocal cord dysfunction and lung tumor (4,13). In our study, two patients (2.4%) were diagnosed with vocal cord dysfunction and a lung tumor.

An increase in the number of chronic diseases and life expectancy emphasizes the importance of the concept of "quality of life". Even though there are many studies evaluating the quality of life in conjunction with other chronic diseases, there are not many studies that have determined the quality of life in pediatric patients with chronic cough. In a multicenter study performed by Chang et al. (12) with 346 patients (average age of four and a half years), the quality of life in patients with chronic cough was found to be lower than in children with other chronic diseases (diabetes mellitus, obesity, cardiac disease, and gastrointestinal disease). They did not compare QoL scores between patients and healthy children before and after treatment. Newcombe et al. (9) developed a chronic cough-specific quality of life measurement tool for children and they found that the quality of life of children with chronic cough was impacted. Other studies concentrate on the quality of life of children with asthma and their caregivers. In a recently published study; İbrahim et al. (22) found that uncontrolled asthma was associated with poor quality of life in asthmatic children and their caregiv-

ers. Similarly, Battula et al. (23) found that newly diagnosed and treated asthmatic children and their caregivers showed a significant improvement in quality of life. In our study, the QoL scores for the patients in the pre-treatment period were significantly lower than in the control group (p= 0.000 for parent TSS; p= 0.021 for patient TSS). This could be due to disruptions in their daily lives, disruptions in their friendships, limitations in their physical ability, poor sleep quality, and low academic success. After the cough was resolved, the patients' QoL scores improved and reached the level of the control group (p= 0.334 for parent TSS; p= 0.458 for patient TSS). There was no significant difference in QoL scores between patient groups with different diagnoses, according to our findings. This may be related to the limited number of patients and the inclusion of different age groups in the study.

A systematic review of 25 studies found that children with asthma, one of the most common causes of chronic cough, had higher anxiety levels (24). This is the first study in the literature to assess and compare the anxiety levels of children with chronic cough prior to treatment and after cough resolution. The anxiety level in patients was found to be significantly higher than in the control group both in the pre-treatment period and after the resolution of cough (p= 0.000 and p= 0.008, respectively). After the resolution of cough, it was observed that the anxiety levels of the patients continued to be higher than those of the control group. Although the symptoms of the patients improved, their anxiety levels remained high; this may be due to the anxiety associated with recomplaint, the presence of a chronic disease, such as asthma, in most patients, and early evaluation of their anxiety level. Further research is required to assess anxiety levels over a much longer post-treatment period.

Limitations

The limitations of our study are as follows: It is a single-center study, reflecting only a six-month period of patient care, and the anxiety level was evaluated at the end of the first month after the resolution of cough. Since our hospital is a tertiary pediatrics hospital, our patients represented a more selected population, which may not be representative of the general pediatric population. There is no validated chronic cough-specific questionnaire for children in our native language, we must, therefore, rely on a general health-related one. Nevertheless, we believe that our study will contribute positively to the literature because it is a prospective study, it includes a follow-up with patients performed in accordance with the ACCP guidelines, and our study adds information to limited data about the quality of life and anxiety level of patients with chronic cough both in the pre-treatment period and after the resolution of cough. It also compares those scores with scores from a control group.

CONCLUSION

Chronic cough may be due to various diseases such as asthma, PBB, and UACS in childhood. Quality of life is impaired in children with chronic cough. In addition, the anxiety level of these patients continues to increase after symptoms improve, and it continues to be higher than in healthy children. It is important to pay attention to the follow-up of patients with chronic cough.

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Ethical Committee Approval: This study was approved by the University of Health Sciences, Ankara Child Health and Diseases Hematology Oncology Training and Research Hospital Ethics Commitee (8.6.2017/082) and informed consent was obtained by patients.

CONFLICT of INTEREST

The authors have no conflicts of interest to declare for this study.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: AİÇ, AG, EDM, ÖŞÜ

Analysis/Interpretation: AG, AİÇ, GC, ZG

Data acqusition: AİÇ, ZG

Writing: AİÇ, AG, MT, EC

Clinical Revision: AİÇ, AG, ÖŞÜ, ZG, MT

Final Approval: All of authors

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