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Is the six-minute walk test correlated with disease control and quality of life in children with asthma?

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Aim: To evaluate the changes in a 6-min walk test (6MWT) and quality of life (QoL) before and after asthma control is achieved in children. A 6MWT is used in the determination of disease severity in many chronic childhood diseases.

Materials and methods: Thirty-six asthmatic children, aged 6 to 15 years, were enrolled before asthma control was achieved. Disease severity parameters during the previous 3 months were recorded. All of the children completed an asthma control questionnaire (ACQ) and received a symptom score; a 6MWT was performed during enrollment and 1 month later, when asthma control was achieved.

Results: The initial and follow-up mean 6MWT distances were 500.2 ± 139.1 and 577.8 ± 147.9 m, respectively ($P < 0.001$). The 6MWT distances and ACQ scores were significantly correlated initially (rho = –0.35, $P = 0.04$). The 6MWT distance was not correlated with clinical parameters ($P > 0.05$ for all). The initial ACQ score was significantly correlated with the symptom score and duration of asthma (rho = 0.62 vs. rho = –0.37).

Conclusion: A 6MWT may be used in the functional assessment of children with uncontrolled asthma; it correlates with ACQ scores. The absence of a correlation between the 6MWT and patient-reported symptom severity or other clinical parameters may indicate the necessity to include a functional assessment into the clinical evaluation as well as QoL measures.

Key words: Asthma, six-minute walk test, asthma control, child

Introduction

The 6-min walk test (6MWT) is a performance-based test to assess exercise tolerance over time that has been shown to be valid and reproducible in many different cardiopulmonary disease states (1-4). In adults with chronic obstructive pulmonary disease, it has been shown to correlate with morbidity and mortality, and in children with cystic fibrosis, it has been reported to correlate with some clinical parameters (5,6). Moreover, 6MWT results were determined to be lower in children with chronic disease states as compared to healthy peers (7). Therefore, the acceptability of the 6MWT has also been demonstrated in children (7,8). It measures the responses of all of the systems during exercise but does not provide information on each system involved in exercise tolerance (9). It is reported to evaluate the submaximal level of exercise capacity, since patients determine the pace rate themselves, but since most daily activities are performed at a submaximal exercise capacity, it is reported to reflect the daily functional state of the patient (9). The test has also been shown to be valid for use in functional capacity assessment in ill children (10). Exercise capacity is the most common functional deterioration in children with asthma. This deterioration in exercise capacity is expected to influence the quality of life (QoL). Therefore, exercise capacity may be used as a functional parameter in the determination of asthma control status.

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The new concept of asthma treatment both in children and adults focuses on "control" and QoL measures, which are important patient-reported outcome measures that provide rational ways to determine asthma control (11,12). One of these questionnaires, an asthma control questionnaire that was developed by Juniper et al., aims to measure the adequacy of asthma control (13). Therefore, it is essential to combine the functional and clinical parameters of disease control with patient-reported outcomes.

The aims of this study were to evaluate the changes in the 6MWT and QoL before and after asthma control was achieved in children and to assess the correlation among the 6MWT distance, asthma control questionnaire (ACQ) score, and patient-reported disease severity score.

Materials and methods

Subjects

Included in the study were 36 children (17 male, 19 female), aged 6-15 years, who had moderate asthma and clinical findings of uncontrolled asthma. Diagnosis of asthma was based on a history of recurrent cough and wheezing with prolonged expiration time, which demonstrated clinical reversibility with short-acting bronchodilator therapy by a beta-2 agonist (11).

Study design

At the beginning of the study, all of the children enrolled were asked to fill out the ACQ and symptom score forms. Moreover, they were asked about the number of acute asthma symptom episodes, days of hospitalizations, days of bronchodilator use, and systemic requirement during the previous 3 months. After all of the information was gathered, a 6MWT was performed by all of the participants. One month after asthma control was achieved, when the patient was clinically stable and lacking acute asthma symptoms, the ACQ was filled out again and another 6MWT was performed.

The study was approved by the institutional ethics committee and written informed consent was obtained from the children and their parents before enrollment in the study.

Six-minute walk test

A 6MWT was performed according to the guidelines of the American Thoracic Society (9). The patients were tested in a 20-m-long quiet and empty hallway and the same hallway was used for all of the 6MWTs, considering that the layout of the track can influence the results (5). The patients were allowed to rest for 10 min before the test was initiated. They were then instructed to walk at a pace that they could tolerate, and it was explained that the aim of the test was to measure the maximal distance that they could walk in the 6-min time period. The test was self-paced and the children were allowed to rest if they could not tolerate the walking, but the time continued to run. Vital parameters including pulse rate and blood pressure were measured before and after the test. The tests were performed under the supervision of one of the pediatricians in the study. The pediatrician instructed the child to start walking at the beginning of the test. He informed the patient of each minute that passed and counted each lap that the patient finished.

Asthma control questionnaire

The ACQ, developed by Juniper et al., aims to assess the adequacy of asthma control and is composed of 7 questions (13). Of the questions, 5 are about the symptoms of asthma during the previous 7 days and 1 is about inhaled bronchodilator use during the same time period. The last question is about predicted forced expiratory volume in 1 s (FEV1)%, which is assessed by clinical staff. However, because this study included children aged 6-15 years, and since most of the children did not cooperate with the spirometry adequately, this last question was not assessed in our study. It has been shown that shortened versions of the ACQ, omitting the FEV1 question, were also valid in clinical trials (14).

Patient-reported asthma symptom score

The asthma symptom score that was used in this study included 6 items reflecting chronic asthma symptoms, such as dyspnea, tightness in the chest, daytime wheeze, nocturnal wheeze, and daily performance during the previous 3-month period (15). Scoring of the items increases from 0 to 3 as the severity increases. The total score is expressed as the sum of all of the scores of the items.

Statistical analysis

Statistical analyses were performed using SPSS 13.0 (SPSS, Chicago, IL, USA). Nonparametric tests were used in the analysis because the values were widely distributed both for the 6MWT and ACQ results. The Wilcoxon signed-rank test was used to compare the 6MWT and ACQ results before and after the achievement of asthma control. Spearman's correlation analysis was performed to assess the correlation among the ACQ results, symptom score, and 6MWT distance. Moreover, correlations of other disease severity parameters with the ACQ results, symptom score, and 6MWT distance were performed with Spearman's correlation analysis.

Results

Characteristics of the study population

The mean age of the children included in the study was 9.8 years with a standard deviation of 2.6 years. The mean duration of asthma was 5.1 ± 3.8 years. During the previous 3-month period, the mean days of inhaled bronchodilator usage and systemic steroid requirements were 3.8 ± 4.8 and 1.3 ± 2.4, respectively. The mean number of episodes of acute asthma symptoms was 0.9 ± 0.9 and the mean number of days of hospitalizations was 0.5 ± 1.3. The mean asthma symptom score was 4.6 ± 2.9 during acute asthma symptoms (Table 1).

6MWT before and after asthma control was achieved

The mean distance of the 6MWT at the initial evaluation was 500.2 ± 139.1 m, whereas after the achievement of asthma control, it was 577.8 ± 147.9 m. There was a significant increase in the distance walked after asthma control was achieved when compared to the initial evaluation (P < 0.001) (Figure 1, Table 2).

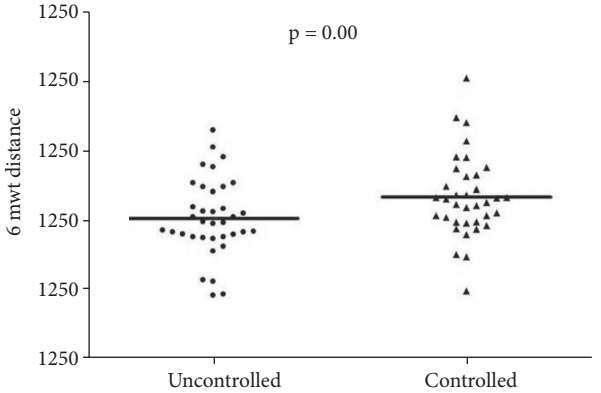

Figure 1. Distribution of the 6MWT results before and after the achievement of asthma control.

ACQ scores before and after asthma control was achieved

There was a significant decrease in the ACQ scores after asthma control was achieved when compared to the initial evaluation (1.6 ± 0.8 vs. 0.3 ± 0.5, P < 0.001) (Figure 2, Table 2).

Correlation of the ACQ, clinical parameters, and 6MWT

There was a significant correlation between the 6MWT distance and the ACQ score during the initial evaluation (rho = –0.35, P = 0.04). However, the 6MWT distance was not significantly correlated with any of the clinical parameters assessed, including symptom score, bronchodilator and systemic steroid requirement, number of episodes of acute asthma findings, and days of hospitalizations during the

Table 1. Disease characteristics of the study subjects (n = 36).

	Mean ± SD
Age (years)	9.8 ± 2.6
Duration of asthma (years)	5.1 ± 3.8
Asthma symptom score in the previous 3 months	4.6 ± 2.9
Days of bronchodilator requirement in the previous 3 months	3.8 ± 4.8
Days of systemic steroid requirement in the previous 3 months	1.3 ± 2.4
Number of acute asthma symptom episodes in the previous 3 months	0.9 ± 0.9
Days of hospitalization in the previous 3 months	0.5 ± 1.3

Table 2. Mean ACQ and 6MWT results before and after the achievement of asthma control.

	Uncontrolled	Controlled	P*
6MWT distance (m)	500.2 ± 139.1	577.8 ± 147.9	0.000
ACQ score	1.6 ± 0.8	0.3 ± 0.5	0.000

*Wilcoxon signed-rank test.

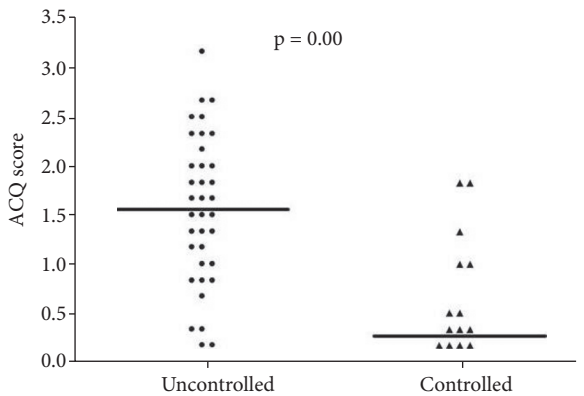

Figure 2. Distribution of the ACQ scores before and after the achievement of asthma control.

previous 3 months (rho = –0.13, –0.24, –0.13, –0.16, and –0.19, respectively). Similarly, there was no correlation between the age of the child or duration of asthma and the 6MWT distance (rho = 0.33 and rho = 0.26, respectively). On the other hand, the ACQ score during the initial evaluation was significantly correlated with the symptom score and duration of asthma (rho = 0.62 vs. –0.37).

After asthma control was achieved, the correlation of the 6MWT with the ACQ score was not significant (rho = 0.01). There was no significant correlation between the changes in the 6MWT distances and the ACQ scores before and after the achievement of asthma control (rho = 0.01).

Discussion

Current asthma treatment relies primarily on the "control" concept (11). This includes functional and clinical assessments as well as patient-reported outcomes (12). A 6MWT is a reliable and valid tool to assess the functional exercise tolerance of children, and the ACQ is a valid tool to assess asthma control (1,7,8,13,14). Both parameters are expected to be impaired in children with uncontrolled asthma. Considering that childhood asthma is a reversible condition with clinical assessment parameters completely normal between exacerbations, these parameters would be expected to improve with the achievement of asthma control. Many previous studies have evaluated the changes in 6MWT results in children with chronic diseases including cystic fibrosis; however, there are no studies that have evaluated the change with asthma control (6,7).

Changes in the 6MWT have been evaluated in the treatment of different diseases, including endothelin-1 antagonist therapy in pulmonary hypertension cases, and the validity and reliability of the test has been demonstrated (8,16). Uncontrolled asthma would be expected to deteriorate functional exercise tolerance. The results of our study indicated a significant improvement in the 6MWT and QoL scores of children after the achievement of asthma control when compared to the initial values. This result emphasizes the functional impairment associated with uncontrolled asthma. Since the functional status of the child is related to his or her daily activities and interaction with friends, it would be expected to influence the QoL.

The correlation of QoL with clinical parameters has been assessed in many diseases with contradictory results (1,4,16-19). In our study, the 6MWT distances and ACQ scores were significantly correlated at the beginning of the study when the children had uncontrolled asthma. This was similar to the results of previous studies (1,4,16). In a study on adult asthma patients, the ACQ scores and 2-min walking test results were shown to correlate significantly (1). In another study on patients with pulmonary hypertension, a correlation was demonstrated between the 6MWT and QoL scores (16). Additionally, the 6MWT results were found to

be correlated with another QoL measure, the short-form 36 health survey, in patients discharged from the hospital after acute respiratory distress syndrome (4). Moreover, in patients with bronchiectasis, the 6MWT was found to be significantly correlated with QoL scores but not with the extent of disease detected by computerized tomography (20). On the contrary, a significant correlation was detected between lung function tests, QoL, and 6MWT results (19). All of these results suggest that the 6MWT is significantly correlated with QoL measures but not with other clinical assessment parameters.

Although the 6MWT result and the ACQ score at the initial evaluation were significantly correlated in our study, the changes in these 2 outcome measures were not correlated when retested after the acute stage. This was similar to the results of a previous study on patients with pulmonary hypertension receiving endothelin-1 antagonist treatment, which reported that 6MWT distances and QoL scores were significantly correlated at all time points but that the change in these 2 outcome measures were not correlated (16). The lack of correlation between the changes in the 6MWT distances and QoL scores identifies that the QoL is not influenced only by a state of physical well being but is also influenced by many other aspects of an individual's health status, including psychosocial factors. The lack of correlation between changes in the ACQ scores and 6MWT results might also be due to a threshold of difference in functional measurements that existed for the change to be noticed by the patients as an improvement, as suggested in a previous study on chronic obstructive pulmonary disease (COPD) (17). Moreover, we did not detect a significant correlation between the 6MWT distances and ACQ scores after the achievement of asthma control. This was mostly attributed to the ACQ scoring system, which yielded 0 in asymptomatic patients.

At the beginning of the study, the patient-reported asthma severity score was significantly correlated with the QoL score but not with the 6MWT results. This finding, emphasizing that patient-reported outcomes may not correlate completely with functional outcome measures, is important considering that the aim of recent asthma guidelines are control-based asthma treatment, necessitating the integration of both parameters in evaluation (11). Previous research about the correlation of functional performance-based exercise tolerance tests reported conflicting results (1,8,21,22). A study performed on adults with chronic obstructive disease or chronic asthma,demonstrated a significant correlation between the 6MWT results and perceived exertion and breathlessness (21). This difference may be partly explained by the different study populations: children with moderate asthma and adults with chronic airway obstruction or severe chronic asthma (21). Asthma in children has completely reversible clinical findings, whereas COPD and chronic severe asthma do not. This might have led to differences in the perception of patients of their symptoms. However, similar to our study, research on adult asthmatics demonstrated a significant correlation between the 6MWT results and asthma severity scores with multivariate analysis (1). Neither the asthma severity score nor the 6MWT result was shown to be significantly correlated with lung function test results in a group of patients with cystic fibrosis (22). However, another study on adults with cystic fibrosis demonstrated a correlation of the 6MWT distances with clinical parameters including body weight and maximal expiratory pressure (8). These different findings are important in emphasizing that functional exercise capacity assessment provides a different aspect of evaluation than either patient-reported outcome measures or clinical assessment parameters.

The limitations of this study include the relatively low number of patients and the large range of ages. However, age was not detected to be correlated with the 6MWT results, and therefore it was not thought to influence the results. Moreover, the addition of a healthy control group would have aided in comparisons. However, the aim of the study was to compare the children with themselves during and after acute asthma symptoms; therefore, a healthy control group was not included.

In conclusion, the 6MWT may be used in the functional assessment of children with uncontrolled asthma, and the results of this test correlate well with ACQ scores. Both evaluation measures improved after asthma control was achieved. The absence of a correlation between the 6MWT distance and patient-reported symptom severity, as well as other clinical disease severity parameters, may indicate the necessity of including a functional assessment in the clinical evaluation, as well as QoL measures.

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