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Three-Minute Step Test to Assess Exercise Capacity in Children With Cystic Fibrosis With Mild Lung Disease

I. Narang, MRCPCH, S. Pike, MCSP, M. Rosenthal, MD, MRCPCH, I.M. Balfour-Lynn, MD, and A. Bush, MD, FRCPCH*

Summary. The information obtained from a simple submaximal test (the 3-min step test) was compared with that from a maximal cycle ergometry study, in a group of children with CF with relatively mild abnormalities of lung function ($FEV_1 > 50\%$ predicted). Nineteen subjects with CF undertook both exercise tests on the same day. Measurements included heart rate (HR), oxygen saturations (SaO_2), visual analogue score of perceived breathlessness (VAS), 15-count breathlessness score (15c), and peak oxygen consumption (VO_2). There were significant differences in the median changes in HR and VAS during the cycle test compared to the step test, 78 vs. 46 beats per minute ($P < 0.05$) and 51 mm vs. 42 mm ($P < 0.05$), respectively. There were no differences between median changes in 15c and SaO_2, but 3 subjects had significant desaturations (>4%) during the cycle test only. Significant exercise desaturations may occur in mild CF lung disease and will not be detected by a 3-min step test. The 15c did not discriminate between a maximal and a submaximal test, and was less useful than VAS. Important information may be missed by the step test which is detected by more complex exercise tests. **Pediatr Pulmonol. 2003; 35:108–113.** © 2003 Wiley-Liss, Inc.

Key words: exercise; cystic fibrosis; desaturations; breathlessness scores.

INTRODUCTION

Physical activity is a natural event in the lives of children, and exercise plays a holistic role in chronic lung diseases such as cystic fibrosis (CF). Exercise testing can provide important information for gauging the impact of many childhood and adolescent diseases. It has been shown to enhance sputum clearance,[1] and as such is an important adjunct to physiotherapy. It improves functional status[2,3] and enhances well-being.[4] Higher levels of exercise performance in formal exercise tests in CF are associated with prolonged survival,[5] leading to the suggestion that exercise testing may be a valuable tool for determining functional status and prognosis in CF.

There are numerous exercise tests validated in chronic respiratory diseases. The 3-min step test has proven useful in the assessment of exercise tolerance in CF patients prior to lung transplantation.[6] Similarly, the 3-min step test has been used to show an improvement in exercise tolerance following a 2-week course of intravenous antibiotics in children with CF with pulmonary exacerbations.[7] More specifically, it is stated that exercise hypoxia can be assessed by the use of this test,[8] and has been used in outdoors high-altitude exercise testing.[9] The modified shuttle test will assess chronic obstructive pulmonary disease in adults,[10] and aid in the diagnosis of exercise-induced bronchospasm in asthmatic and nonasthmatic patients.[11] The Wingate anaerobic test assesses anaerobic fitness in various disease states, and more maximal tests involve the use of cycle ergometry or a treadmill with expired gas analysis.[12,13] An informative exercise test must be able to answer the clinical question being asked and have predetermined valid markers as outcome measures. Such measurements may include heart rate (HR), oxygen saturations (SaO_2), oxygen consumption, and effective pulmonary blood flow. Other parameters that are useful adjuncts to exercise testing include measures of breathlessness, not only an important symptom of respiratory disease but also one of the main limitations to exercise in healthy and diseased individuals. CF patients typically undergo an annual assessment, including lung function and a large number of other tests. Some form of exercise testing has been recommended as part of this

Department of Paediatric Respiratory Medicine, Royal Brompton Hospital, London, UK.

At the North American Cystic Fibrosis Conference (Orlando, Florida, 2001), this work was described in the oral presentation "Step Test Versus Maximal Cycle Ergometry in the Assessment of Exercise Tolerance in Children With Cystic Fibrosis."

*Correspondence to: A. Bush, Department of Paediatric Respiratory Medicine, Royal Brompton Hospital, Sydney Street, London SW3 6NP, UK. E-mail: a.bush@rbh.nthames.nhs.uk

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program.[14] Such a test needs to be quick, simple, and convenient if it is to be applied in large clinics. However, simplifying tests may lead to important information being missed. The aim of this study was to contrast the information obtained from a simple submaximal test (the 3-min step test) with that from a maximal cycle ergometry study, to assess what useful information could be obtained from a 3-min step test.

MATERIALS AND METHODS

Subjects

All subjects were regularly attending the pediatric CF clinics at the Royal Brompton Hospital. They had a confirmed diagnosis of CF,[15] and had forced expired volume in 1 second (FEV_1) of greater than 50% of predicted for gender and height. The subjects were required to be above 8 years of age in order to be able to coordinate the maneuvers on the respiratory mass spectrometer, and have a height greater than 125 cm so that they could reach the pedals on the bike. Exclusion criteria were infection with *Burkholderia cepacia*, coexisting insulin-dependent diabetes mellitus, and resting oxygen saturations of less than 90%. The concurrent use of intravenous antibiotics or additional oral antibiotics, inhaled corticosteroids, and beta agonists was documented.

Ethics

The Royal Brompton Hospital Ethics Committee gave its approval for this study. Written informed consent was obtained from all parents of children taking part in this study, along with assent from the children themselves.

Study Design

All subjects performed the 3-min step test and cycle ergometry test on the same day, with a minimum of 1 hr between the two tests. SaO_2 and HR were continuously monitored during both tests. The visual analogue score of perceived breathlessness (VAS) and 15-count breathlessness score (15c) were measured prior to and after each test. The outcome measures were maximum fall in SaO_2, and a maximum change in HR, VAS, and 15c. In addition, we measured peak oxygen consumption (VO_2) during cycle ergometry.

ABBREVIATIONS

CF	Cystic fibrosis
FEV_1	Forced expiratory volume in 1 second
15c	Fifteeen-count breathlessness score
HR	Heart rate
SaO_2	Oxygen saturations
VAS	Visual analogue score of perceived breathlessness
VO_2 peak	Peak oxygen consumption

Methods

Height (Harpenden Height Stadiometer, Holtain, Ltd., Crymmych, UK), weight (SECA, Birmingham, UK), and FEV_1 were recorded on arrival. Spirometry was performed using a compact portable spirometer (Vitalograph, Buckingham, UK), calibrated before each set of measurements with a 1-liter syringe. Three technically acceptable maneuvers were performed, and the maneuver with the largest FEV_1 was recorded as percentage predicted for gender and height.[16]

Visual Analogue Score

This consists of a 10-cm horizontal line with two anchor points, one at each extreme. On the left (zero) it is labelled, ‘‘I am not at all short of breath.’’ At the other end (10 cm) it is labelled, ‘‘The most short of breath I have ever been.’’ Subjects put a horizontal mark through the line where they think their breathlessness fits on this scale, which is then measured (in millimeters) from the zero point.

Fifteen-Count Breathlessness Score

The subject takes a deep breath and counts out loud to 15, taking about 8 seconds to do so. The number of breaths needed to complete the count, including the initial breath, is the score, the minimum score being one.[17]

Exercise Testing

All subjects performed both the 3-min step test and cycle ergometry. The tests were performed on the same day, with a minimum of 1 hr between the two tests in order to minimize any muscle fatigue prior to the second exercise test. The subjects did not have their exercise tests assigned randomly.

Three-Minute Step Test

The subjects had continuous SaO_2 and HR monitored by pulse oximetry throughout the test using a finger probe (Nellcor, Hayward, CA), which was attached to the index finger. Subjects stepped up and down a commercially available single-step test as in previous studies,[8] set at a height of 15 cm (6 inches). The stepping procedure was demonstrated to the subject prior to the onset of exercise. The stepping rate was 30 per minute for 3 min, and this was controlled by a metronome. Subjects could stop if they felt tired or if the SaO_2 fell below 75%, in which case the total number of steps taken was recorded. The subjects were shown how to change the leading leg to reduce localized muscle fatigue, and standardized encouragement was given.

Cycle Ergometry and Respiratory Mass Spectrometry

The ambient pressure, temperature, and percent humidity were recorded and entered into the respiratory mass spectrometer. The ambient temperature was never greater than 26°C. During maneuvers, the subject had continuous pulse rate and arterial oxygen saturation measured, using a surface oximeter (Nellcor) placed over the right supraorbital artery. Detailed descriptions of the protocols were described elsewhere.[12] Briefly, the subject exercised using an electromagnetic bicycle (Seca 100, Birmingham, UK), which produces a constant workload independent of pedal speeds over the range of 6–150 revolutions per minute. The subject started exercising by cycling initially backwards at zero load to warm up for 1 min, and then forwards, initially at 25 W/m^2, increasing in 15-W/m^2 increments every 3 min until exhaustion, heralded by rocking or progressive speeding up and slowing down on the cycle. During the last 20 seconds of each 3-min exercise stage, the children performed a 12-second rebreathing maneuver while continuing to pedal. For consistency, children were encouraged to pedal at 50–70 rpm during the entire duration of the exercise. At the end of exercise, subjects were disconnected, in order to do the 15c and VAS scores. They were then connected again and remained attached to the mass spectrometer for 9 min to obtain recovery measurements. At the end of this time, the patient was disconnected from the saturation monitor and the mass spectrometer.

Respiratory Mass Spectrometry

An Innovision 2000 quadrupole mass spectrometer (Odense, Denmark) was used to sample subjects' ventilated gas and analyze it on the basis of its mass:charge ratio to determine oxygen consumption. The hardware and physiological measurements are fully described elsewhere.[12,13]

Data Analysis

For the purpose of this study, only the curves related to oxygen consumption during exercise, as measured by the mass spectrometer, were analyzed.

The mass spectrometer software uses algorithms from the above methods to calculate the data. However, to minimize error, all traces were scrutinized to see if there was any evidence of leak around the mouthpiece, i.e., whether the subject inhaled room air during breathing. All such problems were easily identifiable. The data were analyzed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 9.0. Mann-Whitney tests were used to compare changes in outcome measures for the two tests. Spearman's correlation coefficient was used to see if correlations existed between the variables measured and FEV_1.

RESULTS

The subject variables are shown in Table 1. Nineteen children (8 males) performed both tests. Thirteen of these subjects performed the cycle ergometry test first, and 6 performed the step test first. The variables measured are summarized in Table 2.

The median change (range) in the HR (Fig. 1) in beats per minute after the step test was 46 (31–67), compared to a median change of 78 (43–120) after cycle ergometry. This was statistically significant ($P < 0.05$). The median change in VAS (Fig. 2) after the step test was 42 mm (3–56), and after cycle ergometry, 51 mm (22–92). These differences in change in VAS were statistically significant ($P < 0.005$). However, the median change in the objective assessment of breathlessness (the 15c score) was 1 (range, 0–3) after the step test, and 1 (range 0–5) after the cycle test; this was not statistically significant (Fig. 3). There was no significant difference between SaO_2 after the two tests; after the step test, the median change (range) was −1 (−4, +1), and after cycle ergometry, the median change (range) was −1 (−15, +5) (Fig. 4). There was no evidence of an order effect for the exercise tests. The use of antibiotics, inhaled corticosteroids, and beta agonists were independent of any changes observed. Further, using Spearman's correlation coefficient, there were no significant correlations between FEV_1 and SaO_2, HR, VAS, 15c, exercise time on cycle, and VO_2 peak. Using VO_2 peak as a measure of aerobic fitness, neither FEV_1 (Fig. 5) nor exercise time on the bike could predict aerobic fitness. However, 3 subjects significantly desaturated (fall in SaO_2, >4%). during cycle ergometry. Two subjects desaturated from 99% to 84%: one after 3.5 min of exercise, and the other after 11 min of exercise. These subjects were asked to stop pedalling and were disconnected from the respiratory mass spectrometer. Both subjects had spontaneous recovery of SaO_2, and supplemental oxygen was not required. The third subject desaturated from 99% to 93% after 10.5 min of exercise. This subject continued to exercise, and he did not desaturate further. There were

TABLE 1— Variables of Subjects

Number of subjects	Male:female	Median age (range), years	Median FEV_1 % predicted (range)	Median time on cycle, min (range)	Median height, cm (range)	Median weight, kg (range)
19	8:11	13.0 (10.1–16.0)	75 (51–99)	9.0 (3.0–14.3)	148.0 (133.5–169)	37.5 (28.0–56.0)

TABLE 2— Heart Rate (HR), Oxygen Saturations (SaO_2), Visual Analogue Score (VAS), and 15-Count Score (15c) for Step Test and Cycle Ergometry

	Step test	Cycle test
Median resting HR, min (range)	104 (74–129)	91 (70–118)
Median change HR, min (range)*	46 (31–67)	78 (43–120)
Median resting SaO_2, % (range)	98 (94–100)	99 (94–100)
Median exercise SaO_2, % (range)	97 (91–99)	98 (84–100)
Median change SaO_2, % (range)	−1 (−4, +1)	−1 (−15, +5)
Median resting VAS, mm (range)	4 (0–23)	8 (0–44)
Median change VAS, mm (range)*	42 (3–56)	51 (22–92)
Median resting 15c	1	1
Median change 15c (range)	1 (0–5)	1 (0–3)

*$P < 0.05$.

no discriminating variables among these 3 patients, including FEV_1, age, or exercise time on the cycle, that could have predicted change in SaO_2 during exercise (Table 3).

DISCUSSION

The significant desaturations in 3 subjects during cycle ergometry are a surprising finding. Further, these episodes were not manifested during the 3-min step test and could not be predicted. It is not known what effect this would have, if any, on their exercise performance, as exercise was terminated. However, significant hypoxia will limit oxygen available for oxidative phosphorylation in exercising muscles and cause premature muscle fatigue and thus limitation of exercise. It could be that this group of subjects limits itself to lower-intensity exercise subconsciously and therefore, as in these cases, do not recognize any limitation of exercise ability. We also need to determine why these subjects desaturate during exercise. There certainly were no variables common to all 3 subjects that could have allowed us to predict these changes. One possible explanation to account for these findings is ventilation perfusion inequality causing a reduction in the efficiency of gas transfer during high-intensity exercise. One would expect these changes to worsen with progression of the disease process, and this group of subjects may benefit from annual exercise tests to monitor this. Other possible explanations include a shunt and diffusion limitation. In the former case, blood enters the arterial system without going through ventilated areas of lung; if this is severe enough, it can result in hypoxaemia. In the latter case, the diffusing capacity of the lung increases because of increases in both the diffusing capacity of the membrane and the volume of blood in the pulmonary capillaries. These changes are brought about by recruitment and distension of pulmonary alveolar capillary units. If, by some mechanism, this is not achieved, diffusion limitation may account for a decrease in the partial pressure of arterial oxygen.

However, in some patients, an increase in oxygen saturations from baseline during exercise was observed. This is thought to be secondary to paradoxical bronchodilation in patients with CF during exercise. Not surprisingly, the change in VAS and HR was greater after the cycle test compared to the step test, as the former test is of greater intensity and duration. However, the 15c was the same for both tests, and therefore independent of

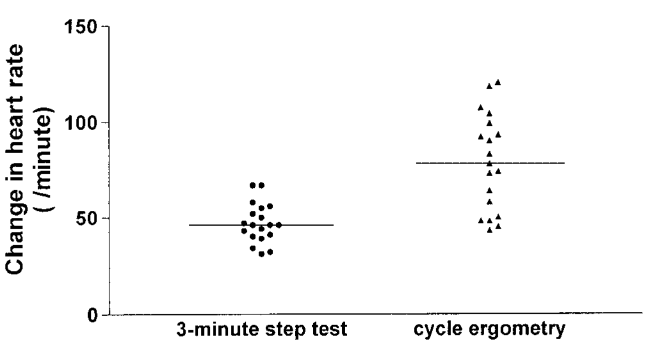

Fig. 1. Absolute changes in heart rate (per minute) after step and cycle ergometry tests. Horizontal lines represent median values. There was a significant difference between the two tests ($P < 0.05$).

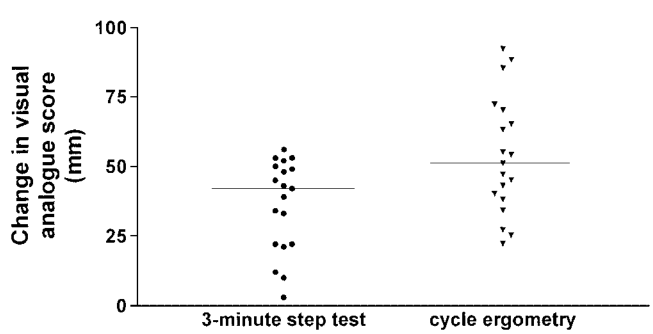

Fig. 2. Change in visual analogue score (in millimeters) after step and cycle ergometry tests. Horizontal lines represent median values. There was a significant difference between the two tests ($P < 0.05$).

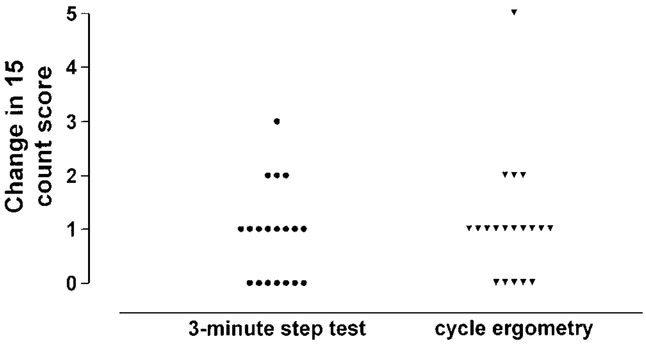

Fig. 3. Changes in 15-count scores after step and cycle ergometry tests. There was no significant difference between the two tests ($P > 0.05$).

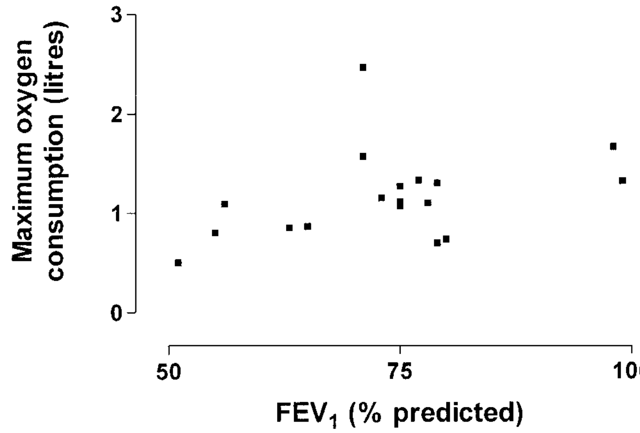

Fig. 5. Maximum oxygen consumption vs. FEV_1 (% predicted) in all subjects. There was no correlation between maximum oxygen consumption and FEV_1 ($r = 0.33$).

exercise intensity and duration. In contrast to a recent study[17] where the 15c could differentiate degrees of breathlessness induced by exercise of varying intensities in children with CF, the subjects in the present study clearly felt more breathless at higher-intensity exercise as depicted by the VAS, but this was not detected by the 15c score. This could be partly explained by the motivation of these patients to achieve low 15c scores, as their perception of this score equated with health and fitness.

Although the clinical utility of maximal values is limited, the submaximal phases equate with normal levels of physical activity and allow valid interpretations to assess those factors that limit exercise performance on a day-to-day basis. One difficulty when conducting a study that compares two exercise tests is the effect of fatigue upon the results of the second test. Although there was lack of randomization for exercise testing, the present study allowed at least 60 min between tests. There was no statistically significant difference between resting HR and resting SaO_2 between the two tests. Further, there was no order effect that would account for the differences shown.

Previous studies examined different tests of similar intensities to assess exercise performance in cystic fibrosis.[6,8] However, this study showed that there is limited information to be gained by performing a low-intensity test in a group of children with mild lung function. However, an incremental step test might have been useful to compare incremental phases during cycle ergometry.

In this group of children with CF who have relatively well-preserved lung function, the 3-min step test provided limited information relating to exercise performance. While it is neither practical nor suitable to perform maximal cycle ergometry with expired gas analysis on every patient attending outpatient clinics, a suitable exercise test to assess exercise performance of these patients must be of a higher intensity and equate more to normal levels of physical activity. This exercise test must be able to provide clinically relevant information longitudinally. The most appropriate test may vary with stage of the disease. While it is known that dyspnea will limit exercise performance, the use of the 15c as an adjunct to exercise testing has not been shown to be discriminatory.

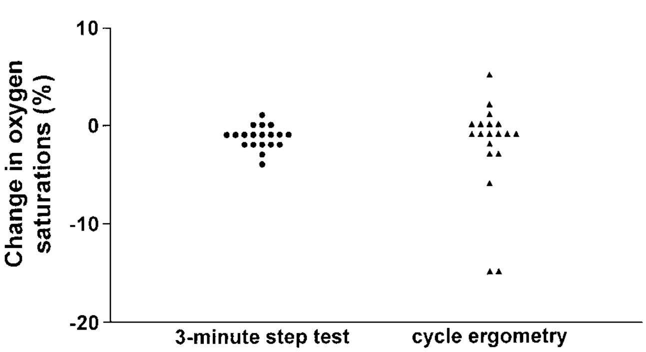

Fig. 4. Absolute changes in arterial oxygen saturations (%) after step and cycle ergometry tests. There was no significant differences between the two tests ($P > 0.05$).

TABLE 3— Details of 3 Subjects Who Desaturated During Cycle Ergometry

	Patient 1	Patient 2	Patient 3
Age (years)	11.8	14.5	14.8
Resting SaO_2, %	99.0	99.0	99.0
Lowest SaO_2, %	84.0	84.0	93.0
FEV_1 (% predicted)	80.0	73.0	78.0
Change in VAS, mm	70.0	34.0	27.0
Change in 15c	0.0	1.0	1.0
Exercise time (min)	3.5	11.0	10.5

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