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UPDATE OF THE BRONCHIAL CHALLENGE TEST WITH EXERCISE

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ABSTRACT

The bronchial challenge test with exercise (BCTE) aims to demonstrate the presence of exercise-induced bronchial hyperreactivity, characteristic of bronchial asthma. Its realization is well standardized, requiring special environmental conditions, preparation and submaximal effort of the patient. The response is measured by spirometry, and a decline in 10% of the expired volume at the first second (FEV1) would be considered as a positive challenge test with exercise. This article describes the elements necessary to facilitate this test, according to national and international standards and guidelines.

Key words: bronchial hyperreactivity, exercise, bronchial challenge test, children.

INTRODUCTION

The BCTE is an indirect test that acts by stimulating the release of mediators in the bronchial mucosa, a pathophysiological mechanism similar to that occurring in asthma. This response to exercise triggers bronchial smooth muscle contraction, which is called exercise-induced bronchoconstriction (EIB). On that basis, indirect tests are more specific for the diagnosis of asthma, but generally less sensitive than direct tests (1-3).

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The objective of the BCTE is to demonstrate the presence of bronchial hyperreactivity, which is indicated with the measurement of the forced expiratory volume at the 1st second (FEV1). (4). It is suggested to measure the response with FEV1 and not MEF (maximum expiratory flow) due to its greater repeatability and reproducibility (5).

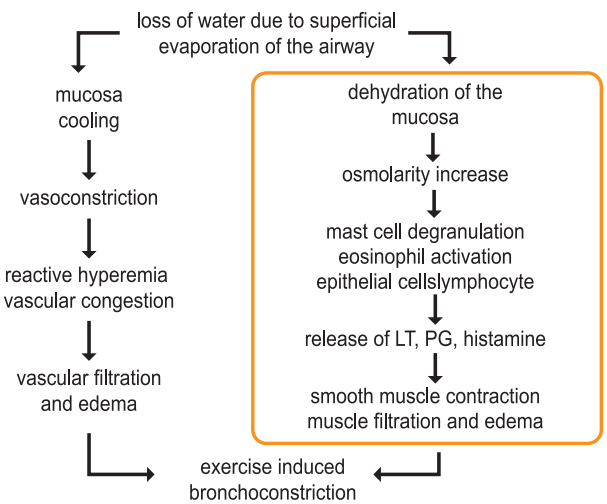
EIB does not necessarily occur in the presence of bronchial asthma, it is present in 10-18% of the general population, in 30-70% of elite athletes and in 30-90% of patients with persistent asthma (1,2). Its symptoms could include coughing, wheezing, chest tightness or respiratory distress related to exercise, which are not asthma specific (4). In regards to bronchial asthma, according to the cut-off point chosen for FEV1 decline, its sensitivity varies between 40-60%, and its specificity 70-90% (4,6,7).

PATHOGENESIS OF EXERCISE-INDUCED BRONCHOCONSTRICTION

Although the mechanism is not fully clarified, the most accepted theories refer to the changes produced in the airway due to hyperventilation (Figure 1). Increasing the respiratory rate increases the inspiration of a larger volume of relatively cold and dry air, since when using the nose clip the patient breathes through the mouth. The respiratory mucosa loses heat and moisture, resulting in increased osmolarity on its surface. This causes the activation of mast cells and epithelial cells, which release pro-inflammatory factors such as histamine, leukotrienes, prostaglandins and other cytokines that stimulate the bronchial muscle. Inhalation of cold air also causes vasoconstriction, followed by reactive hyperemia, with bronchial vascular congestion, edema and therefore a decrease in airway caliber. (Figure 1) (1,3,8,9).

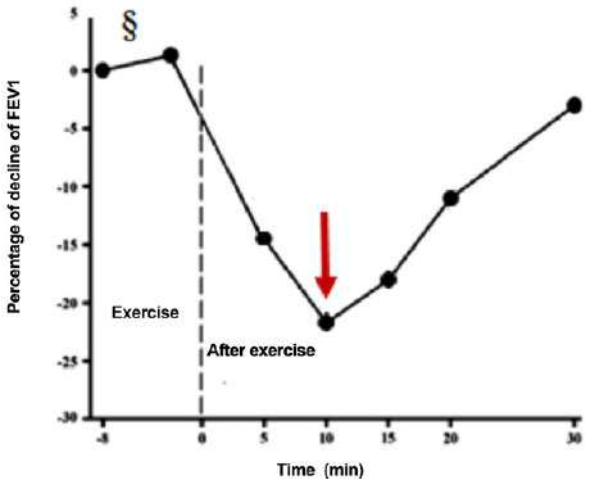
The main determinants of the expression of the response and severity against exercise are the water content and the temperature of the inspired air and the level of ventilation achieved and maintained (3,4,7).

Figure 1. Pathophysiological mechanisms of exercise induced bronchoconstriction.



Durante el ejercicio la vía aérea muestra una leve dilatación inicial, aumentando los valores del VEF1. Posteriormente aparece la broncoconstricción que es máxima frecuentemente entre los 2 y 5 minutos después de finalizar el ejercicio. Este broncoespasmo cede espontáneamente, alcanzando las cifras basales a los 30-60 minutos. En el laboratorio esta broncoconstricción se revierte con mayor rapidez utilizando un broncodilatador (10) (Figura 2).

Figure 2. FEV1 measurements during the bronchial challenge test with exercise in an asthmatic child.



In this example it can be seen that the FEV1 increases slightly in regards to the baseline during exercise (§). After the 6-8 minute run the FEV1 declines in more than 10% (red arrow) and recovers spontaneously after 30 minutes.

INDICATIONS

The main indication for the BCTE is to demonstrate the presence of EIB in asthmatic patients with a history of respiratory distress, cough, respiratory noise or choking sensation related to exercise. It is also indicated to control the effectiveness of the maintenance treatment, and adjust its dosage according to response.

On the other hand, it is helpful to differentiate EIB from other causes of exercise-related symptoms, the most frequent being of laryngeal origin, such as vocal cord dysfunction (8,11).

CONTRAINDICATIONS

- Lack of collaboration or understanding of the procedure
- Patient with bronchial obstruction
- Due to the risk of severe bronchoconstriction, it is recommended that the FEV1 prior to the exam be ≥ 75% and the SpO2 ≥ 93% (2)
- Intense exercise within the previous 4 hours (refractory period)
- Heart disease (mainly arrhythmias), high blood pressure
- Neuromuscular or orthopedic disease
- Fever
- Uncontrolled insulin dependent diabetes
- Uncontrolled epilepsy (2,8)

PATIENT PREPARATION

The patient should come dressed in comfortable clothes and sneakers, and have consumed a light diet. In addition, the patient should not have exercised intensely during the 4 hours prior to the appointment since evidence shows that 50% of patients with EIB are refractory to a second test after 1 hour. Most lose this state at 2 hours, but occasionally it can last up to 4 hours (1,2,8).

Drug suspension (Table 1)

The indication of suspending the patient's maintenance treatment is at the discretion of the physician requesting the test. In regards to Montelukast, it begins to protect the airway after 2 hours from being administered with a duration of its effect from 12-24 hours (4). Inhaled corticosteroids show protection after 1 week of continuous use (4).

Table 1. Medication suspension time.

Medication	Suspension Time
Short-acting β agonists: salbutamol, terbutaline	6 hrs
Long-acting β agonists: salmeterol, formoterol	36 hrs
Long-acting β agonists: indacaterol, olodaterol, vilanterol	48 hrs
Short-acting muscarinic antagonists: Ipratropium bromide	12 hrs
Long-acting muscarinic antagonists: tiotropium, glycopyrrolate	7 hrs
Leukotriene receptor antagonists (montelukast, zafirlukast)	12 hrs - 4 days
Oral Theophylline	12-24 hrs
Chromone	4 hrs
Caffeine	24 hrs
Non-steroidal anti-inflammatory drugs (ibuprofen, indomethacin)	3 days

The suspension of antihistamines is also left to the discretion of the attending physician. It is suggested to suspend 72 hours before the test, however it has been seen that loratadine, cetirizine, fexofenadine do not affect test results (12-14). Caffeine consumption decreases bronchial reactivity produced with exercise, so the patient should not ingest this product at least 24 hours prior to the exam. Foods that contain caffeine are tea, coffee, coca-cola, chocolate (15,16).

All medications that the patient is receiving at the time of the test must be recorded in the report.

PROCESS

The test is carried out in the pulmonary function laboratory, under controlled humidity and temperature and environmental conditions, ideally 50% and 20-25 ° respectively. These may vary but must be located within the area shown in the nomogram (Figure 3) (4). The patient must use a nose clip to cause loss of water in the airway.

The use of a treadmill is preferred rather than a bicycle since the increase in ventilation is faster. This should reach 40-60% of the maximum voluntary ventilation (estimated as FEV1 x 35). To facilitate the evaluation of the intensity of the exercise, the heart rate (HR) replaces the measurement of ventilation (3.11). This should reach a submaximal level that is calculated using the formulas in Table 2. In children, the HR should increase by at least 85%, with a maximum of 95%. The second formula, published recently, is more accurate (11). HR should be monitored continuously with thoracic tape (for example Polar® tape) or a pulse oximeter. The person's fitness level and body weight will influence the level and speed to achieve the expected HR. The duration of the exercise is 6 to 8 minutes, and the submaximal HR must be kept constant for at least the 4 final minutes. The degree of inclination and the speed of the treadmill are established once this level of effort is reached. It is suggested to start with an inclination of 3 °, increasing maximum up to 10 ° and speed 3.6 miles / hour (1-3.8).

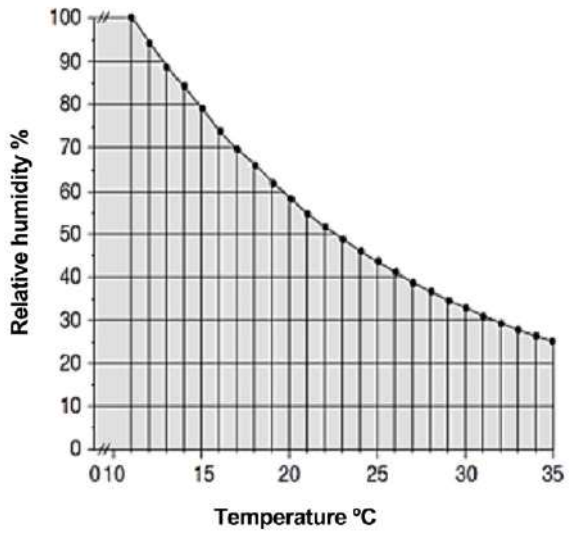
ASSESSMENT OF THE RESPONSE

The performance and interpretation of a post exercise baseline spirometry should follow the corresponding recommendations (17). Flow / volume and volume / time curves should be recorded to control the quality of the maneuvers.

Table 2. Formulas to calculate Cardiac Frequency during submaximal exercise test (FCsm)

FCsm = (220-age) x 85 to 95%
FCsm = 208 – 0,7 x age

Figure 3. Environmental conditions.



The shaded area represents the ideal conditions to perform the exercise test (1)

The variable used is FEV1, since it shows greater repeatability and reproducibility than Maximum Expiratory Flow (MEF) (1,5,8). In patients of preschool age, the FEV0.5 measurement can be used (18). A complete FVC maneuver is not required, it is enough for the patient to exhale 1 second. 2 or 3 FEV1 (or FEV0.5) (4.5) must be obtained, choosing the highest value measurement. The suggested scheme to measure FEV1 post exercise is: 3,5,10,15,20 and 30 minutes after the end of exercise performance. Measurements can be added per minute if the patient has distant audible wheezing or another sign of respiratory distress (4,5,8,19,20).

The way to calculate the decline in FEV1 (or FEV0.5) is:

$$\% \text{ of decline of FEV1} = \frac{\text{baseline value- decline value}}{\text{decline value}} \times 100$$

Once the measurements are completed, if the patient has a positive response, 400 µcr of salbutamol should be administered and spirometry repeated to confirm respiratory functional normality.

The test should be stopped in case of: audible wheezing from a distance, significant dyspnea, vasovagal symptoms, chest pain, desaturation. The presence of wheezing and SpO2 should be recorded.

Positivity criteria

In healthy children, a maximum decline in FEV1 is approximately 4% (6.7). In schoolchildren, a decline in FEV1≥ 10-15% (2-4.6-8) is considered a positive response. A 10% decline gives greater sensitivity and specificity similar to the use of a 15% decline (1,6). The suggested cut-off point is 10%. In preschoolers, a decline in FEV0.5 of 13% is considered positive (18).

False negative

The most frequent causes that keep from not achieving the required submaximal HR are environmental conditions that do not favor bronchoconstriction (heat, higher humidity). There may also be false negatives in patients who perform intense exercise prior to the test (refractory period) and who have not suspended the use of β-adrenergic agents.

False positive

The most frequent cause is the lack of spirometry effort. Also consider a differential diagnosis: exercise-induced laryngeal dysfunction, the most frequent being vocal cord dysfunction (11).

SECURITY MEASURES

In the latest standardization by the European Society (ERS 2018) (2) it is recommended that blood pressure and electrocardiogram be monitored. Because ECG registration during the procedure is difficult to meet in most pulmonary function laboratories, it is suggested that the patient have a 3-channel ECG if there is no suspicion of heart disease and 12 channels if there is suspicion, before conducting the study (2). In addition, SpO2 must be registered continuously. After inhaling with a bronchodilator, FEV1 should return to at least 90% of the baseline. The technician or doctor who performs the test should be able to detect signs of bronchial obstruction and respiratory failure. It is imperative to have a crash cart (2).

REPORT

Exam Description

Report the baseline spirometry, record the baseline FEV1, environmental conditions (room temperature and humidity), baseline heart rate and post exercise, baseline SpO2 and post exercise. Write down any medication that the patient has received on the day of the test. Describe the used spirometry and test protocol. It is suggested to show the FEV1 response according to Table 3.

Only describe what is observed in the test and express the conclusion as follows:

- "there was no significant bronchoconstriction"
- "there was mild-moderate-severe bronchoconstriction"

Table 3. FEV1 response report.

Time	3 min	5 min	10 min	15 min	20 min	30 min
FEV1 (L)						
% Decline						

FEV1 per minute is optional.

Graduation of the severity of bronchoconstriction: (5)
- Mild: FEV1 decline ≥ 10% and <25%
- Moderate: FEV1 decline ≥ 25% and <50%
- Severe: FEV1 decline ≥50%

SPECIAL CONSIDERATIONS

Elite athletes

If the exercise test is normal consider other tests (methacholine test, eucapnic hyperventilation). The criteria for evaluating EIB should be based on the specific sport, in the environment in which it is done, and the test should be carried out with the intensity that the athlete uses in effort in competition. If the BCTE is carried out in the laboratory, it is suggested to consider a decline in FEV1 of 7% (1,20).

Bronchial challenge test with free range running

If you do not have a treadmill free range running could take its place. It is not reproducible like the laboratory test but is much more sensitive (21). It is useful in screening for EIB, although it is complex to standardize environmental conditions and comply with the safety measures suggested by international guidelines (2, 22). Environmental conditions can increase the development and severity of the EIB, by inhalation of allergens or pollutants (4).

The variable to be measured must be FEV1. The duration of the run and HR are similar to those described above. The HR is measured before and after the run, the latter should not be interrupted. If the patient has significant bronchoconstriction, the interpretation should consider the environmental conditions in which the stimulus was performed (pollen, environmental pollutants, temperature and humidity). A 15% drop in FEV1 is considered significant. In the case of not having a spirometer, an MEF fall of 15% could be considered (3).

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