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Cough, a vital reflex. Mechanisms, determinants and measurements

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Summary. Cough is a natural defense mechanism that protects the respiratory tract from inhaling foreign bodies and by clearing excessive bronchial secretions. As a spontaneous reflex arc, it involves receptors, an afferent pathway, a center processing information, an efferent pathway and effectors. The determinant factor of cough efficacy is the operational volume of the lung, which in turn relies on the strength and coordination of respiratory and laryngeal muscles as well as on lung mechanics. Respiratory muscle weakness and dysfunction as well as expiratory flow limitation and lung hyperinflation may occur in some neuromuscular disorders and in obstructive airway diseases, respectively. Accordingly, all these diseases may show an ineffective cough. In this brief overview, we deal with the determinants of the cough efficacy and the clinical conditions affecting cough efficacy as well as the cough's efficacy measurements in clinical setting. (www.actabiomedica.it)

Key words: cough, cough peak flow, neuromuscular disorders, chronic obstructive pulmonary disease

Cough is a natural defense mechanism that along with mucociliary clearance, bronchoconstriction and phagocytosis can effectively protect the respiratory tract from inhaling foreign bodies and by clearing excessive bronchial secretions (1).

Cough may be a voluntary act or a spontaneous reflex arc and in this case involves receptors, an afferent pathway, a center processing information, an efferent pathway and effectors. The receptors are placed throughout the bronchial tree and, although in a lesser extent, also in other areas: ear, paranasal sinuses, pleura, diaphragm, pericardium and esophagus. From receptors the afferent impulses are channeled through the vagus nerve in the medulla oblongata, where they are processed. Then, efferent impulses are conveyed by motor nerves and reach the effectors, which are the respiratory and laryngeal muscles.

Schematically, we may distinguish four different phases of cough, as a vital reflex arc, the first of which is a part in the afferent pathway while the last three in the efferent one (2):

1. *Receptorial phase:* there is the stimulation of cough receptors that are activated and, accordingly, send an impulse to the center through the vagus nerve;
2. *Inspiratory phase:* that consists in a wide opening of the glottis by contraction of the arytenoid cartilage with rapid inhalation, which involves an average of 50% of vital capacity with wide variations in relation to the stimulus and the type of receptors;
3. *Compressive phase:* that consists in a prompt closure of the glottis following the contraction of the adductor muscles of the arytenoid cartilages with consequent adduction of the vocal cords. At the same time, there is a strong contraction of the abdominal muscles and other expiratory muscles resulting in an increased intrapulmonary pressure and compression of the alveoli and bronchioles.
4. *Expiratory phase:* in this final phase, vocal cords and epiglottis open suddenly for action of the

abductor muscle of the arytenoid cartilages, thereby causing the explosive leakage of air from the lungs to the outside. Subsequently, the exhalation continues, favored by the complete relaxation of the diaphragm.

In this brief overview, we deal with the determinants of the cough efficacy and the clinical conditions affecting cough efficacy as well as the cough's efficacy measurements in clinical setting.

Determinants of cough efficacy

Since the result of the cough reflex arc is the production of an airflow, the determinant factor of cough efficacy is the operational volume of the lung (3), which in turn relies on the strength and coordination of respiratory and laryngeal muscles as well as on lung mechanics.

The weakness and/or the incoordination of the respiratory and/or laryngeal muscles may significantly decrease the driving pressure applied to the alveoli and to the bronchial airways. The reduction in driving pressure consequently results in low expiratory volumes and flows during cough. A weakness or a dysfunction of the respiratory muscles are common conditions in many neuromuscular disorders (Table 1). At the same time the impairment of laryngeal muscles, either in terms of strength or coordination, can significantly limit the development of compression phase and the following increase in intrapulmonary pressure.

Tabella 1. Neuromuscolar desease with respiratory muscle weakness

Diseases of the Central Nervous System	• Parkinson's disease • Quadriplegia • Multiple sclerosis • Poliomyelitis • Motor neuron disease
Peripheral neuropathies	• Guillain-Barré syndrome • Charcot-Marie-Tooth disease
Myasthenia	• Myasthenia gravis • Lambert-Eaton syndrome
Muscular dystrophies	• Duchenne dystrophy • Myotonic dystrophy
Toxic myopathies	• Alcoholic myopathy • Steroid myopathy

The decrease of operational volume of the lung can be the consequence not only of a weakness of respiratory muscles, but also of the expiratory flow limitation and lung hyperinflation. These pathophysiological features may occur in some obstructive airway diseases, such as chronic obstructive pulmonary disease (COPD), cystic fibrosis, bronchiectasis, tracheomalacia and asthma. Accordingly, all these diseases may be associated with cough inefficacy (1). Expiratory flow limitation and lung hyperinflation may result from different mechanisms, such as bronchoconstriction and/or an impairment of elastic recoil of the lung.

Measurements of cough efficacy

Cough efficacy can be measured by means of the gastric pressure (P_{ga}), as well as the peak flow (CPF) and exhaled volume (CEV) at the mouth during a voluntary and maximal cough (4) (Figure 1).

P_{ga} is measured using a commercially available latex balloon catheter, which is inserted through the nose and positioned in the stomach. The balloon catheter is connected to a manometer and the subject is asked to perform 3-6 coughs, starting from maximal inspiration. In normal subjects, Pga values are greater than or equal to 100 cmH2O in women and 130 in men cmH2O (5). The measurement of P_{ga} is an invasive test, which on the other hand enables to directly measure the driving pressure, developed by the synergistic contraction of the abdominal muscles during cough.

The CPF is assessed while the subject coughs in a tightly fitting full-face mask, adherent to patient's face and connected to a computerized pneumotachograph, starting from maximal inspiration. The test is repeated 3-6 times. Healthy individuals of both sexes develop CPF values greater than or equal to 360 L/min (4). Patients with values of CPF under 160 L/min have a quite ineffective cough and require manually assisted cough and/or mechanical insufflation-exsufflation (4).

CEV can be measured together with CPF assessment. In healthy individuals, CEV values are usually greater than 1 L with an average value of 2.4 L (6).

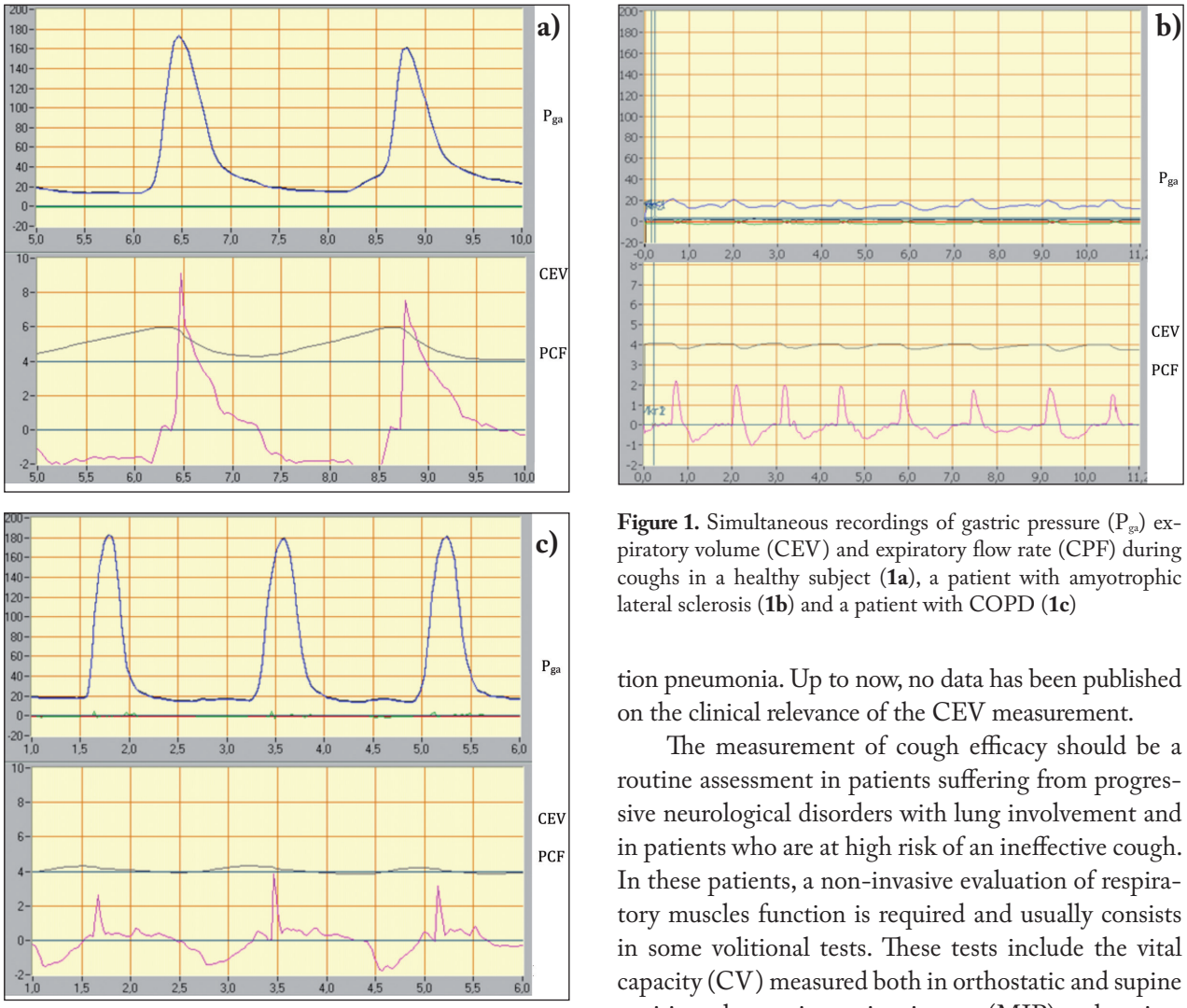

Figure 1. Simultaneous recordings of gastric pressure (P_{ga}) expiratory volume (CEV) and expiratory flow rate (CPF) during coughs in a healthy subject (**1a**), a patient with amyotrophic lateral sclerosis (**1b**) and a patient with COPD (**1c**)

CPF evaluation is clinically relevant and it can be considered an overall parameter of cough efficacy (7). Neuromuscular patients with values of CPF less than 270 L/minute are at risk of retention of bronchial secretions and respiratory failure in case of bronchial infection (8). Interestingly, as shown in a study in patients with Multiple Sclerosis (9), the cough efficacy as measured by CPF significantly correlates with the disability status calculated by means of Expanded Disability Status Scale (EDSS). In patients with stable amyotrophic lateral sclerosis, CPF <4.25 L/sec could also predict the risk of ineffective spontaneous cough during a respiratory tract infection (10). Moreover, a recent study (11) has shown that in patients with acute stroke, higher values of CPF are associated with a low risk of secondary aspiration pneumonia. Up to now, no data has been published on the clinical relevance of the CEV measurement.

The measurement of cough efficacy should be a routine assessment in patients suffering from progressive neurological disorders with lung involvement and in patients who are at high risk of an ineffective cough. In these patients, a non-invasive evaluation of respiratory muscles function is required and usually consists in some volitional tests. These tests include the vital capacity (CV) measured both in orthostatic and supine position, the maximum inspiratory (MIP) and expiratory (MEP) mouth pressures, the nasal pressure during a sharp, maximal and short (less than 0.5 seconds) sniff maneuver, which is a complementary test to MIP (4). The mouth pressure during a maximal whistle is a volitional, non-invasive test, which may be considered as a complementary test to MEP (12) and is particularly useful in children having difficulties to perform MEP manoeuvre (13). Non-volitional and invasive tests may be required in non-cooperative patients or in patients providing non-univocal results at volitional tests (4). Moreover, in case of a documented impairment of respiratory muscle function, an arterial blood-gas analysis may be requested to ascertain whether a hypoxemic-hypercapnic respiratory failure due to a ventilatory pump impairment may occur.

Patients with a decreased operational volume of the lung due to an obstructive ventilatory defect and lung hyperinflation show a reduced forced expiratory volume at 1st second (FEV1)/CV ratio and an increase in the Residual Volume (RV)/Total Lung Capacity (TLC) ratio. In these patients, the CPF and CEV reduction may also occur without a reduction of the P_{ga}, as a consequence of a normal driving pressure (Figure 1c).

Conclusions

In clinical practice, it is a common experience that infections of the respiratory tract are the most frequent causes of morbidity and mortality in patients with neuromuscular diseases, as well as in patients with broncho-obstructive diseases.

Cough is a reflex arc, which acts as a defensive physiological mechanism against the inhalation of foreign bodies and the pathogens of the respiratory tract. In order to produce an effective cough, an operational volume of the lung should be in the normal range and this fact involves a normal function of the respiratory and glottis muscles as well as requires normal lung mechanics.

In order to improve cough efficacy in neuromuscular patients, devices capable of assisting both the inspiratory and the expiratory phase of cough and of improving the operational volume of the lung are now available. Notably, in bulbar and in non-bulbar ALS patients, mechanical insufflation-exsufflation can significantly increase air flow during cough (14). Moreover, in patients with COPD the use of bronchodilators, such as beta2-agonists or muscarinic antagonists, can significantly reduce the exacerbation rate and this effect might be linked to an improvement in operational volume of the lung and, accordingly, to a more effective cough.

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