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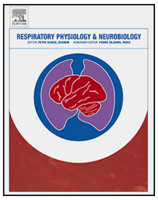

Determinants of cough effectiveness in patients with respiratory muscle weakness

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ABSTRACT

Experiments were undertaken to mechanistically define expiratory-muscle contribution to effectiveness of cough while controlling glottic movement. We hypothesized that electrical abdominal-muscle stimulation in patients with respiratory-muscle weakness produces effective coughs only when glottic closure accompanies coughs. In ten spinal-cord-injury patients, esophago-gastric pressure and airflow were recorded during solicited-coughs, coughs augmented by abdominal-muscle stimulation, and passive open-glottis exhalations. During solicited-coughs, patients closed the glottis initially; five were flow-limited, five non-flow-limited. Stimulations during solicited-coughs or open-glottis exhalations elicited similar driving pressures (changes in gastric pressure; $p < 0.001$). Despite high driving pressures, stimulations induced flow-limitation only when patients transiently closed the glottis – not during open-glottis exhalations. That is, transient glottic closure enabled transmission of abdominal (driving) pressure to the thorax during cough, while impeding dissipation of intrathoracic pressure. In conclusion, transient glottic closure is necessary to render cough effective in patients with respiratory-muscle weakness, indicating that failure to close the glottis contributes to ineffective cough in weak tracheostomized patients and patients with bulbar disorders.

1. Introduction

Cough plays a major role in problems experienced by patients with a wide variety of respiratory diseases (Dicpinigaitis et al., 2012), especially patients with neuromuscular disorders (Laghi and Tobin, 2003). Our understanding of the integrated physiology of cough, however, is rudimentary. Cough is a complex respiratory movement involving mucus, and coordinated recruitment of inspiratory muscles, expiratory muscles and the glottis (Hasani et al., 1994; Lasserson et al., 2006; Polkey et al., 1998; Smith et al., 2012). The goal of this coordinated activity is to generate high intrathoracic pressure when the glottis closes briefly during a cough (Knudson et al., 1974; Ross et al., 1955). High intrathoracic pressure is necessary to induce dynamic airway compression – a key factor in achieving effective cough (Estenne et al., 1994). This combination (high intrathoracic pressure and transient compression of the airway) facilitates the achievement of a flow of air at high linear velocity through the airways (Knudson et al., 1974; Kulnik et al., 2016). The high velocity of air transfers kinetic energy to intraluminal secretions, shearing them off the bronchial wall and carrying them towards the mouth (Ross et al., 1955; Sivasothy et al., 2001). Transient airway compression also promotes development of turbulent expiratory flow, which creates additional shear forces, contributing to the dislodgement of secretions (King et al., 1985; Zahm et al., 1991).

In patients with airway obstruction, forced expectoration while the glottis is open – so-called huffing – is as effective as cough in clearing radioactive particles (Hasani et al., 1994; Sutton et al., 1983) and expelling mucus (Hasani et al., 1994). The effectiveness of this open-glottis maneuver likely rests on the achievement of high transpulmonary pressure (Langlands, 1967), which generates a flow of air at high linear velocity through the airways. High transpulmonary pressure cannot be achieved by expiratory muscle contraction in patients with respiratory muscle weakness

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(Laghi and Tobin, 2003). This consideration raises the possibility that the effectiveness of cough in patients with muscle weakness may be critically dependent on transient closure of the glottis. Glottic closure prevents dissipation – within the thorax – of abdominal pressure generated by expiratory muscle contraction (the driving pressure for cough).

Isolating and defining the precise contribution of expiratory muscle contraction to the effectiveness of cough while concurrently controlling movement of the glottis is impossible in healthy subjects. To overcome this obstacle, we took advantage of an experiment of nature and employed external stimulation of the expiratory muscles in patients with spinal-cord injury. Incremental stimulation of paralyzed expiratory muscles in patients able to voluntarily close their glottis provides a unique opportunity to unravel the mechanistic contribution of abdomino-thoracic pressure in determining whether a cough is effective or not. Stimulations were delivered during a solicited cough (when the glottis is closed transiently), and during a passive exhalation (when the glottis is open). We defined the effectiveness of cough in operational terms: that expiratory muscle contraction (in response to external stimulation) generated an abdominal pressure (the driving pressure for cough), which, following transmission to the thorax, was sufficient to induce dynamic airway compression. Various methodologies have been employed to determine whether dynamic airway compression occurs during cough, such as radiography (Ross et al., 1955), video-endoscopy (Estenne et al., 1994), and pressure-flow relationships (a plot of peak expiratory flow against corresponding esophageal pressure during a cough) (Estenne et al., 1994). The development of a plateau on a flow tracing (of a pressure-flow curve) signifies expiratory flow limitation, and occurs only as a result of dynamic airway compression (Estenne et al., 1994).

The goal of this study was to define mechanistically the contribution of expiratory muscle contraction to the effectiveness of cough while concurrently regulating glottic movements. Specifically, we hypothesized that stimulation of the abdominal muscles in patients with respiratory muscle weakness produces an effective cough only when there is accompanying (transient) glottic closure.

2. Methods

(See online supplement for additional details)

2.1. Patients

Ten patients with spinal-cord injury were recruited (Table 1**)**. Patients were selected if their injury resulted in motor impairment above the seventh thoracic level based on clinical estimation of the neurological impairment (McBain et al., 2013). Exclusion criteria included need for mechanical ventilation or tracheostomy, abdominal pathology that could have interfered with electrode placement and stimulation, and presence of implanted electronic devices such as cardiac pacemakers, defibrillators and intrathecal pumps. The study was approved by the local human studies subcommittee. Written informed consent was obtained from all patients.

2.2. Experimental setup

2.2.1. Flow and pressure measurements

Airflow was measured at the mouth with a heated pneumotachometer connected to a differential pressure transducer. Volumes were obtained by electronic integration of the flow signal.

Esophageal (Pes) and gastric (Pga) pressures were separately measured with balloon-tipped catheters coupled to pressure transducers (Mador et al., 1996). Airway pressure (Paw) was measured at the mouthpiece using a third pressure transducer

2.2.2. Electrical stimulation of the abdominal muscles

Stimulations of the abdominal muscles were delivered by means of surface electrodes. Electrodes were applied using an anterior configuration and anterolateral configuration as previously described (Gollee et al., 2008; Kandare et al., 2002; Langbein et al., 2001) (Fig. 1). We tested two different configurations to determine whether four electrodes (anterior configuration) would suffice to achieve expiratory flow limitation or whether eight electrodes (anterolateral configuration) would be needed to achieve that goal.

An electrical stimulator was connected to the anterior electrodes. A second stimulator was connected to the anterolateral electrodes (Fig. 1). Both stimulators were programmed to generate trains of electrical impulses with a 250 μs pulse width, at a frequency of 50 Hz for duration of 1 s (Butler et al., 2011). During anterolateral stimulations, the two stimulators were linked to deliver the stimulations simultaneously.

Stimulations were triggered once 300 milliseconds of absent inspiratory flow (zero flow or expiratory flow) had elapsed from the manual activation of a handheld switch controlled by an investigator.

The minimum current used with the anterior configuration (4 electrodes) and anterolateral configuration (8 electrodes) was that which caused sufficient abdominal-muscle recruitment to produce a 4 cmH_2O rise in Pga (threshold stimulation) while patients relaxed at end-expiratory lung volume with nose clipped and mouthpiece occluded.

2.2.3. Electromyogram (EMG) abdominal muscles

To assess whether electrical stimulations were properly timed, one pair of surface electrodes was applied over the external oblique (Laghi et al., 2014) (Fig. 1).

2.3. Experimental protocol

Patients were studied while supine with the head of the bed raised 30° from the horizontal position. After placement of all transducers and electrodes, patients were instructed to carry out the following maneuvers.

2.3.1. Maximal expiratory efforts

Patients were instructed to perform at least five maximal expiratory efforts against a valve that could be closed by turning a tap. Maximal expiratory pressure was measured at total lung capacity (TLC).

2.3.2. Unassisted solicited coughs

To determine whether expiratory flow limitation was achieved during unassisted cough, patients performed a series of 12–23 solicited coughs of varying intensity commencing from TLC (Estenne et al., 1994). After each cough, patients were told how strong the next cough should be (Estenne et al., 1994). A 1-to-2 min period of resting breathing elapsed between two successive solicited coughs.

2.3.3. Solicited coughs combined with electrical stimulations of abdominal muscles

To determine whether stimulations combined with solicited coughs could induce expiratory flow limitation, patients performed a series of forceful solicited coughs commencing from TLC while concurrently receiving stimulations using the anterior (10–15 coughs) and anterolateral electrode configuration (9–15 coughs). Stimulator current (mA) was set between 20 and 100% of the current range, starting from the threshold stimulation to the maximum output achievable by the stimulator(s) (100 mA) (Lee et al., 2008).