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ScienceDirect

Neuromuscular Disorders 27 (2017) 518–525

www.elsevier.com/locate/nmd

Twitch mouth pressure for detecting respiratory muscle weakness in suspicion of neuromuscular disorder

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Received 28 July 2016; received in revised form 23 December 2016; accepted 31 January 2017

Abstract

Twitch mouth pressure using magnetic stimulation of the phrenic nerves and an automated inspiratory trigger is a noninvasive, non-volitional assessment of diaphragmatic strength. Our aims were to validate this method in patients with suspected neuromuscular disease, to determine the best inspiratory-trigger pressure threshold, and to evaluate whether twitch mouth pressure decreased the overdiagnosis of muscle weakness frequently observed with noninvasive volitional tests. Maximal inspiratory pressure, sniff nasal pressure, and twitch mouth pressure were measured in 112 patients with restrictive disease and suspected neuromuscular disorder. Esophageal and transdiaphragmatic pressures were measured in 64 of these patients to confirm or infirm inspiratory muscle weakness. Magnetic stimulation was triggered by inspiratory pressures of −1 and −5 cmH_2O. The −5 cmH_2O trigger produced the best correlation between twitch mouth pressure and twitch esophageal pressure ($R^2 = 0.86$; $P < 0.0001$). The best association of noninvasive tests to predict inspiratory muscle weakness was sniff nasal pressure and twitch mouth pressure. Below-normal maximal inspiratory pressure and sniff nasal pressure values suggesting inspiratory muscle weakness were found in 63/112 patients. Only 52 of these 63 patients also had abnormal twitch mouth pressure. In conclusion twitch mouth pressure measurement is a simple, noninvasive, nonvolitional technique which may help to select patients with suspected neuromuscular disorder for invasive inspiratory-muscle investigation.

Keywords: Neuromuscular diseases; Twitch mouth pressure; Respiratory muscle strength; Magnetic stimulation

1. Introduction

Accurately evaluating muscle strength is essential both to the diagnosis of neuromuscular disease (NMD) in patients with lung volume restriction and to the monitoring of respiratory function over time in patients with known NMD. Most patients with NMD experience worsening respiratory dysfunction responsible for recurrent lower respiratory tract infections, sleep disordered-breathing and, eventually, respiratory failure. Moreover, specific molecular therapies for several NMDs are undergoing clinical evaluation, a crucial component of which is an accurate assessment of respiratory muscle strength over time [1,2].

Maximal static inspiratory pressure (MIP) is typically diminished in NMDs, and a normal MIP value rules out clinically significant inspiratory muscle weakness [3]. However, poor coordination or motivation may impair a patient's ability to perform the maneuver required for MIP measurement. Because sniffing is a natural behavior that is often easier to perform, sniff nasal inspiratory pressure (SNIP) can be a helpful complement to MIP [4–6]. Nevertheless, with both tests, inadequate patient cooperation can lead to low values that erroneously suggest inspiratory muscle weakness [7]. Diagnostic accuracy is substantially better with tests that are more complex and/or invasive [8]. Thus, nonvolitional

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http://dx.doi.org/10.1016/j.nmd.2017.01.022
0960-8966/

bilateral anterolateral magnetic stimulation of the phrenic nerves with measurement of twitch transdiaphragmatic pressure (TwPdi) and/or twitch esophageal pressure (TwPeso) has been validated in normal individuals and ambulatory patients [9,10]. However, this method requires the insertion of at least an esophageal catheter [11].

Twitch mouth pressure (TwPmo) measurement has been developed as a non-volitional and noninvasive alternative to TwPeso measurement [12–15]. However, in individuals resting at functional residual capacity (FRC), magnetic phrenic-nerve stimulation can induce upper airway collapse and/or glottis closure, thereby impairing the transmission of pressure changes from the alveoli to the mouth. This problem can be eliminated by gentle inspiratory [14] or expiratory [13] maneuvers during stimulation or by using an automated controlled inspiratory-pressure trigger device [16,17]. This last method has been evaluated in healthy individuals [16,17] and in patients with obstructive lung disease [7,18], but not in patients with restrictive lung disease, in whom global muscle dysfunction may increase the difficulty of maintaining upper airway permeability.

Our primary aim was to validate TwPmo measurement in patients with suspicion of neuromuscular disorder, while determining the best inspiratory-pressure trigger threshold for magnetic stimulation. We also evaluated whether adding TwPmo decreased the number of patients mistakenly diagnosed with severe inspiratory-muscle weakness when combined MIP and SNIP was used alone.

2. Materials and methods

The study was performed between November 2013 and July 2015 at the respiratory physiology department of the Raymond Poincaré Teaching Hospital (Garches, France), in accordance with the amended Declaration of Helsinki. The local ethics committee (CPP Paris Ile de France XI) approved the study (approval number 13036), and written informed consent was obtained from all patients.

2.1. Patients

Consecutive patients referred for evaluation of known NMD or of lung volume restriction with suspected muscle weakness were included. Pregnant women and patients with presence of metallic objects within the field during the impulse (pace-makers, cochlear implants, shrapnel, aneurysm clips, etc.) were excluded [10].

2.2. Measurement protocol

Lung function was tested in the upright and supine positions using the SensorMedics Vmax 229 system (Yorba Linda, CA, USA) according to standard guidelines [19]. MIP and SNIP were then measured from FRC in the upright position. MIP was measured using a flanged mouthpiece, which could be occluded at the distal end with a valve, leaving a small leak to prevent glottis closure during the inspiratory maneuver. SNIP was measured during a sniff maneuver, through an earplug hand-fitted around the tip of a catheter inserted into one nostril and with the other nostril occluded, as previously described [5,20]. The highest values from five MIP and ten SNIP maneuvers were recorded.

TwPmo was measured with the patient seated comfortably and breathing through a flanged mouthpiece and a three-way non-rebreathing valve. The mouthpiece was connected to a #2 Fleisch pneumotachograph (Fleisch, Lausanne, Switzerland) itself connected to a differential pressure transducer (MP45 ± 3 cmH_2O; Validyne Engineering Corp., Northridge, CA, USA) and pressure was inferred using a pressure transducer (MP45 ± 100 cmH_2O; Validyne Engineering Corp., Northridge, CA, USA). After at least a 20-minute rest [21], magnetic phrenic-nerve stimulation was delivered at the neck via a 90-mm circular coil placed over the flexed cervical spine and powered by a Magstim stimulator (Magstim 200, Magstim Co. Ltd., Whitland, UK). Optimal coil position was determined by delivering several stimulations at 70% of maximal output on the midline over the spinal processes at various levels between C5 and C7. All magnetic stimulations were applied at FRC. Each stimulation was delivered when a predetermined inspiratory-pressure trigger (−1 or −5 cm H_2O in random order) was reached, as described previously [18], and we used an analogic comparator designed by our group, which was connected to the differential pressure transducer. Five stimulations were delivered using each trigger level, and the highest value for each was recorded. Magnetic stimulations were separated by at least 30 seconds to avoid potentiation [21]. Forty-five minutes was required to perform SNIP, MIP and TwPmouth measurements.

In patients referred for evaluation of diaphragmatic function, transdiaphragmatic pressure (Pdi) was computed as the difference between gastric pressure and esophageal pressure (Peso) measured using a catheter-mounted pressure transducer system (Gaeltec, Isle of Skye, UK), which have a pressure range between +150 and −150 mmHg. The catheter was inserted through the nose after local anesthesia of the nasal mucosa. Catheter position was assessed by asking the patient to perform sharp sniff maneuvers while observing the signal. The esophageal and gastric transducers were advanced into the stomach until a positive deflection occurred when gentle pressure was applied to the stomach. The catheter was then withdrawn until a sip of water induced a sharp rise in proximal transducer pressure (due to esophageal muscle contraction) with no concomitant change in distal transducer pressure, indicating that the proximal transducer was in the esophagus and the distal transducer in the stomach. An occlusion test was done to assess Peso measurement validity [22]. For the TwPdi measurements, we again used the analogic comparator to activate magnetic stimulation when the predetermined inspiratory pressure trigger (−1 or −5 cm H_2O in random order) was reached, as described previously [18]. Five stimulations were delivered using each trigger level, and the highest value for each was recorded. Magnetic stimulations were separated by at least 30 seconds to avoid potentiation [21]. Airway flow and pressure obtained from TwPmo and TwPdi were sampled at 1000 Hz and recorded using an analogic-numeric system (MP 150, Biopac System, Goleta, CA, USA) with its software (Acknowledge).