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Determination of normal values for an isocapnic hyperpnea endurance test in healthy individuals

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ABSTRACT

Respiratory Muscle Endurance (RME) is an alternative way to assess respiratory muscle impairment but normal values are lacking to use this test in a clinical perspective. Our objective was then to determine reference values of RME in healthy subjects.

We recruited 161 healthy subjects (25–80 years old) who were distributed within 5 groups with a 10-year range. We measured vital capacity (VC) and maximal respiratory pressure (MIP, MEP). The RME test consisted of isocapnic hyperpnea at increasing levels of ventilation until exhaustion to determine Tlim (expressed in minutes and as percentage of maximal voluntary ventilation, MVV).

A significant difference between age-groups was observed for both VC and MEP expressed as percentage of predicted value. Mean Tlim was 21.8 ± 5.9 min [95% confidence interval 20.9–22.8], 74.4 ± 15.9% of predicted MVV [95% CI 71.8–76.9]. Tlim was similar among age groups. Tolerance to the RME test was excellent.

This study provides normal values of RME in a large age range of healthy subjects and demonstrates that RME is preserved in the elderly.

1. Introduction

Assessment of respiratory muscle function is of critical importance in neuromuscular diseases in order to detect earlier respiratory failure and its subsequent morbidity and mortality (Benditt and Boitano, 2013; Lo Coco et al., 2006; Shoesmith et al., 2007). In Amyotrophic lateral sclerosis (ALS) for instance, weakness and fatigue of the respiratory muscles are associated with a loss of compliance of the thoraco-pulmonary system and an increased risk of atelectasis (Hardiman, 2011). Also, an increased respiratory muscle work can precipitate the development of hypercapnia (Begin and Grassino, 1991). The diagnosis of respiratory failure and the initiation of non-invasive positive pressure ventilation to compensate for hypoventilation are based on well-defined clinical, spirometric and blood gases criteria (Andersen et al., 2012). The predictive value of each of these parameters is however low and the occurrence of respiratory muscle weakness is frequently overestimated (Steier et al., 2007). Moreover, indicators used to assess respiratory muscle weakness are not always closely correlated with transdiaphragmatic pressure (Pdi) (Fromageot et al., 2001; Lechtzin et al., 2002; Schmidt et al., 2006).

Respiratory muscle endurance has been defined as the capacity to sustain high levels of ventilation under isocapnic conditions (ventilatory endurance test) (Leith and Bradley, 1976), or to breathe for a prolonged period of time against a known resistance (Jones et al., 1985). The endurance capacity of the respiratory muscles depends on the interaction between the respiratory system impedance and the maximum available muscle power. The maximum time (Tlim) that hyperpnea or inspiratory resistive breathing can be sustained is inversely related to both the level of Pdi generated and the inspiratory fraction of the breathing cycle (i.e. duty cycle), and hence inversely related to their product (i.e. tension-time index of the diaphragm) (Bellemare and Grassino, 1982a,b). Renggli et al. (2008) demonstrated that, in healthy subjects, contractile fatigue of the diaphragm and abdominal muscles

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occurs early during hyperpnoea and that other mechanisms such as impaired central drive may also participate to task failure. Tlim during inspiratory resistive breathing is linked to the predetermined fraction of the maximum inspiratory Pdi at functional residual capacity (Pdi/Pdimax) by a curvilinear relationship. The value of Pdi/Pdimax that could be generated indefinitely is around 0.4 (Roussos and Macklem, 1977). These data suggest that quite high inspiratory loads can be sustained indefinitely and emphasize the need to precisely determine the respiratory muscle load to assess endurance. Although respiratory muscle strength and endurance seem to be strongly correlated, many other parameters, like disuse, treatments, coexistence of chronic respiratory or neuromuscular diseases, are also susceptible to influence endurance (ATS/ERS Statement on respiratory muscle testing, 2002).

A well tolerated method for assessing respiratory muscle endurance consists in sustained heavy breathing at constant or increasing target minute ventilation, i.e. respiratory endurance test, RET (ATS/ERS Statement on respiratory muscle testing, 2002). The objective of RETs is to evaluate the maximum sustainable ventilation (MSV) as a fraction of maximal voluntary ventilation (MVV). Two techniques are available for assessing MSV. In the first one, subjects are asked to breathe at a target minute ventilation of approximately 70–90% MVV during 8 min. The second method described by Mancini et al. (1994) is an incremental RET consisting in hyperpnea at increasing minute ventilation/maximal voluntary ventilation (V_E/MVV). The test begins at a minute ventilation corresponding to a low percentage of MVV and then the level of hyperpnea is increased every 3 min by a fixed fraction of MVV by increasing breathing frequency (BF) (Mancini et al., 1994; Vergès et al., 2009; Villiot-Danger et al., 2011), until the subjects could not sustain the target hyperpnea level (task failure). The minute ventilation during the last 3 min step completed has been suggested to be an index of respiratory muscle endurance (ATS/ERS Statement on respiratory muscle testing, 2002; Mancini et al., 1994). Mancini et al. (1994) clearly showed that both tests provided comparable levels of MSV, providing the last 3 min step of hyperpnea is considered. As part of being a shorter duration test than the original described one, MSV during the incremental RET mimicks peak exercise V_E, for instance in heart failure patients (Mancini et al., 1994). Since this first report, the incremental RET has been successful used in spinal cord injury patients and in obese adults (Vergès et al., 2009; Villiot-Danger et al., 2011). During RETs, normocapnia can be obtained by partial CO_2 rebreathing, which is critical for the good tolerance of these tests.

In the 1980s, the first RET studies determined that the maximal sustainable minute ventilation in healthy subjects was about 60–80% MVV (Keens et al., 1977; Leith and Bradley, 1976). However, no further study has been conducted to standardize respiratory muscle testing by sustained hyperpnea and normal values of RET, lower limit of normal and factors influencing respiratory muscle endurance in health (e.g. age) remain unknown. This precludes the application of RET in clinical practice where standardized evaluation of respiratory muscle endurance is lacking.

Thus, the objective of this work was to establish reference values for respiratory muscle endurance assessed by a RET among healthy subjects in a large range of age.

2. Subjects and methods

2.1. Subjects

Between October 2014 and May 2015 we recruited 161 men and women between 25 and 80 years old through newspaper advertisement. Inclusion criteria were the absence of confirmed neurological or respiratory diseases. A preliminary interview allowed excluding pregnant women, and subjects with neurological or respiratory pathologies, major thoracic deformation, or cardiac disease.

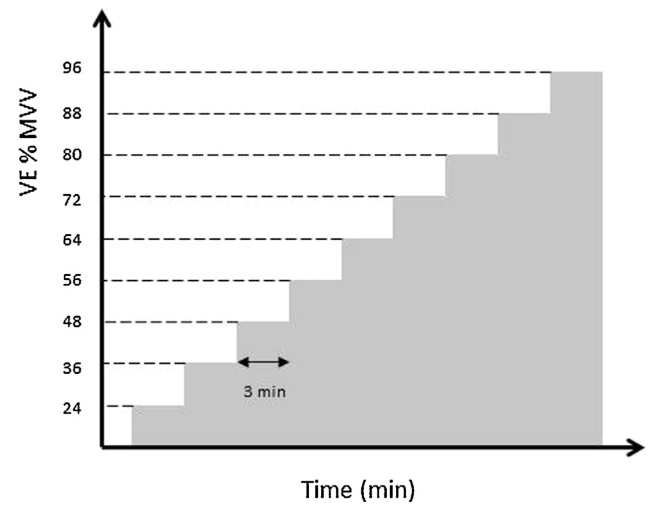

Fig. 1. Description of the incremental hyperpnea protocol used during the respiratory endurance test. Minute ventilation (V_E) was initially adjusted to reach 24% of predicted maximum voluntary ventilation (MVV) and then was increased by 8% MVV every 3 min. Tlim corresponded to the last 3 min step completed.

The institutional ethical review board of our hospital approved the study (ANSM B140667-31) and all participants gave an informed written consent.

2.2. Pulmonary function tests

All subjects underwent standard pulmonary function tests (PFT) and RET on the same day. PFT consisted in measurement of vital capacity (VC), forced expired volume in 1 s (FEV1) and respiratory muscles strength assessment (maximal inspiratory pressure, MIP; maximal expiratory pressure, MEP; sniff nasal inspiratory pressure, SNIP; HypAir, Medisoft, Belgium), according to international recommendations (Miller et al., 2005). Predicted maximal voluntary ventilation (MVV) was calculated as 35 times FEV1.

2.3. Respiratory endurance test

Isocapnic hyperpnoea endurance was assessed by using a Spirotiger® device (Idiag, Fehraltorf, Switzerland). It is a commercially available respiratory muscle endurance training device used in patients for improving respiratory muscle function. It allows partial CO_2 rebreathing, thus assuring normocapnic hyperpnea. RET was performed by adapting an endurance test protocol previously described by Verges et al. (Vergès et al., 2009). Subjects were asked to breathe through a mouthpiece with a nose-clip in place. The mouthpiece was attached to a tube connected to the rebreathing bag and to room air through a valve. The volume of the bag was set at 40% of VC with an adjustable clip and, for the first stage, target V_E was set at 24% of predicted MVV. Then BF was adjusted every three minutes in order to increase V_E by 8% MVV until task failure or until completion of the 96% MVV step (Fig. 1). We adapted the setup from previous reports (Villiot-Danger et al., 2011), based on preliminary tests to ensure feasibility and tolerance of the RET in older subjects. The SpiroTiger® provides continuous feedback for BF and tidal volume (V_T). A visual feedback allowed the subject to maintain a constant V_T, while visual and auditory feedbacks imposed to the subject a target BF. Therefore, the subjects had to follow an imposed breathing pattern throughout the test with constant V_T and progressively increasing BF.