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Work of breathing in children with diffuse parenchymal lung disease

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ABSTRACT

Respiratory mechanics have been poorly studied in children with chronic diffuse parenchymal lung disease (DPLD). The aim of the study was to assess the usefulness of respiratory mechanics to monitor lung function alteration in children with DPLD. Respiratory mechanics, total (WOBt), elastic (WOBe) and resistive (WOBr) work of breathing, gas exchange, lung function and respiratory muscle strength were measured in 10 children, aged 1.8–18.4 years old, who were followed in our national reference centre. Mean tidal volume (V_T) was normal (11 ± 4 mL/kg) but respiratory rate (f_R, 32 ± 19 breaths/min), f_R/V_T (118 ± 75 breaths/min/L) and total lung resistance (10.2 ± 4.8 cm H_2O L^{-1} s) were increased. Mean WOBt was increased mainly due to WOBe. Dynamic lung compliance (C_{Ldyn}) was severely reduced (26 ± 24 mL/cm H_2O). C_{Ldyn} and the oesophageal pressure-time product strongly correlated with vital capacity and functional residual capacity. Respiratory muscle strength was within the normal range. In conclusion, lung mechanics may be considered as useful complementary or alternative markers of functional abnormalities in children with DPLD.

1. Introduction

Diffuse parenchymal lung diseases (DPLD) in children are a heterogeneous group of parenchymal pulmonary disorders with varying causes, histological appearances and outcomes (Clément and Eber, 2008; Clément et al., 2010; Nathan et al., 2011). Because the majority of the diseases included in the terminology DPLD involve inflammatory or fibrotic infiltration of the alveolar walls, common physiological abnormalities are present. These abnormalities have been described mainly in adult patients and include a restrictive ventilatory defect and an impaired gas exchange with a carbon monoxide diffusing capacity (DL_{CO}) which is typically reduced to a greater extent than the lung volume at which it is measured (O'Donnell, 1998; Zapletal et al., 1985). Tidal volume (V_T) is decreased and respiratory frequency (f_R) is increased, mimicking external elastic loading (Gaultier et al., 1982; Lama and Martinez, 2004). Hypoxaemia as defined by a reduced resting arterial oxygen saturation or a reduced resting arterial oxygen tension is often present, while hypercapnia occurs only late in the disease course (Clément et al., 2004). During exercise the above described dysfunctions become even more pronounced (Lama and Martinez, 2004).

Recently, the American Thoracic Society proposed an official clinical practice guideline on the evaluation and management of childhood interstitial lung disease in infancy, and recommend infant pulmonary function testing among other evaluations (Kurland et al., 2013). Moreover, the European Respiratory Society task force on chronic interstitial lung disease stated that even though lung function testing does not provide specific information, it represents a useful tool for both the diagnosis and the management of interstitial lung disease in conjunction with other studies (Clément et al., 2004). However, the functional respiratory

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evaluation is limited in children because most tests require a minimal level of cooperation, which may be impossible or difficult to obtain in young children. In clinical practice, respiratory assessment is thus restricted to global respiratory variables such as gas exchange and parameters that can be measured noninvasively during spontaneous breathing such as functional residual capacity (FRC). The difficulty of breath holding, for the measurement of the DLco, or exercise testing limit the assessment of the severity of the disease and its monitoring.

Respiratory mechanics can be measured quite easily during spontaneous breathing in children by means of a small oesogastric catheter that allows the calculation of numerous respiratory parameters. The aim of the study was to analyze the breathing pattern, respiratory mechanics, and respiratory muscle strength in order to assess the usefulness of these parameters as complementary or alternative markers to monitor functional abnormalities in children with chronic DPLD.

2. Methods

2.1. Patients

The measurements were performed in consecutive patients followed in our centre, which is the national reference centre for paediatric DPLD, Respirare®. In France, rare diseases have been identified as a priority for public health needs, and among the various actions launched a National Reference Centre for Rare Lung Diseases (Respirare®, www.respirare.fr) was created on 2006 to care for all the children in the country suspected or known to have one of them, including DPLD. The parents and the patients gave informed consent for the study which was approved by the Institutional Review Board of the French learned society for respiratory medicine, "Société de Pneumologie de Langue Française" (CEPRO).

2.2. Measurements and protocol

The lung function testing started with the measurement of functional residual capacity using the helium dilution technique (FRCHe) and the mean of two measurements within 10% was retained for analysis (Hyp'air and Master Hyp'air, Medisoft, Sorinnes, Belgium) (McCoy et al., 1995). Interrupter resistance (Rint) measures were performed according to the international recommendations and the mean of a series of at least five acceptable measurements was calculated (Hyp'air, Medisoft, Sorinnes; Belgium) (McKenzie et al., 2002). Results were given as absolute values and as predicted values according to height and gender.

When possible, carbon monoxide diffusing capacity corrected for alveolar ventilation (DLco) was measured using the multiple breath method and expressed as percentage of predicted (Stam et al., 1998). Vital capacity (VC) was measured in the upright position (Morgan Spiroflow spirometer). At least three acceptable VC curves were performed and the curve with the highest VC was registered (Beydon et al., 2007; Miller et al., 2005). Predicted VC values were calculated (Quanjer, 1993).

Blood gases were measured after a 30 min rest using the arterialized capillary technique (Gaultier et al., 1979). Pulse oximetry (SpO_2) was also recorded. Hypoxaemia was defined by a partial arterial oxygen pressure (PaO_2) <−2SD and hypercapnia by a partial arterial carbon dioxide pressure ($PaCO_2$) >+2SD (Gaultier et al., 1979).

Afterwards, the patient remained in the sitting position and breathed room air to achieve a steady state. Breathing pattern was determined from flow tracing, measured by a pneumotachograph (Fleisch #3, Lausanne, Switzerland) connected to a mouthpiece. fR, VT, and minute ventilation (VE) expressed in mL/kg were measured, and the rapid shallow breathing index (fR/VT) was calculated (Yang and Tobin, 1991). Inspiratory (TI) and expiratory (TE) times were calculated as well as inspiratory (VT/TI) and expiratory (VT/TE) flows.

Subsequently, an oesogastric catheter (Gaeltec, Dunvegan, Isle of Skye, UK) was inserted pernasally after careful local anaesthesia (lidocaine 2%, Astra Zeneca, Rueil-Malmaison, France) (Stell et al., 1999). Appropriate placement of the catheter was checked according to the technique of Baydur et al. (1982). The patient was asked to breathe again calmly in room air for at least 5 min. The patient's oesophageal pressure-time product (PTPoes) was then calculated as follows. The PTPoes per breath was obtained by measuring the area under the oesophageal pressure (Poes) signal between the onset of inspiratory effort and the end of inspiration, and was referred to the chest wall static recoil pressure-time relationship according to a methodology adapted from Sassoon et al. (1991). PTPoes was also expressed per minute by multiplying the PTPoes/breath by fR (PTPoes/min) (Field et al., 1984). The total (WOBt), elastic (WOBe), and resistive (WOBr) work of breathing were also calculated using modified Campbell diagrams constructed from pressure and volume data (Cabello and Mancebo, 2006; Cross et al., 2012). In healthy subjects, the work of breathing is around 0.35 J/L (Mancebo et al., 1995), and WOBe and WOBr represent about 2/3 and 1/3 of WOBt, respectively (Cabello and Mancebo, 2006; Peters, 1969). The static pressure–volume curve of the chest wall was estimated using a value of chest wall compliance (Ccw) calculated as 4% predicted vital capacity (Agostoni and Mead, 1964). Dynamic lung compliance (CLdyn) was measured during quiet breathing as previously described (Hart et al., 2002; Mead, 1961). The total lung resistance (R_L) was calculated using the mid-tidal iso-volume method of Frank et al. (1957). Dynamic intrinsic positive end-expiratory pressure (PEEPi) was measured as the amount of negative deflection in Poes preceding the start of inspiratory flow.

Finally, the strength of the inspiratory muscles was measured by asking the patient to perform a maximal sniff manoeuvre. The greatest Poes during a sniff (Sniff Poes) obtained after at least 10 manoeuvres was retained for analysis (Fauroux et al., 2009; Lofaso et al., 2006). The strength of the expiratory muscles was measured by asking the patient to perform a maximal cough. The peak gastric pressure value of at least five maximal coughs (Pgas cough) was measured and the greatest value was selected (Man et al., 2003; Nicot et al., 2006).

The diaphragmatic tension time index (TTdi), which estimates the endurance of the diaphragm, was calculated during quiet breathing as TTdi = (mean Pdi/SniffPdi) × TI/Ttot, where Pdi = transdiaphragmatic pressure during spontaneous breathing, SniffPdi = Pdi during a maximal sniff, and Ttot = total breath time. The oesophageal tension time index (TToes), which estimates the overall endurance of the inspiratory muscles, was calculated as TToes = (mean Poes/Sniff Poes) × TI/Ttot (Bellemare and Grassino, 1982; Zocchi et al., 1993).

All the signals were digitized at 200 Hz and sampled for analysis using an analogue/digital acquisition system (MP 100, Biopac Systems, Goletta, CA), run on a PC computer (Elonex™, Gennevilliers, France) and displayed on Acqknowledge software.

2.3. Statistical analysis

Data are given as mean ± SD. Correlations between parameters were assessed by Pearson or Spearman correlation tests. Comparisons between two groups were performed using the *t*-test in case of normal distribution or the Mann Whitney Rank Sum test otherwise. A *p* value of less than 0.05 was considered as significant.