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Comparison of barometric whole body plethysmography and its derived parameter enhanced pause (PENH) with conventional respiratory mechanics in healthy Beagle dogs

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Abstract

The purpose of the study was to compare barometric whole body plethysmography (BWBP) and its derived parameter, enhanced pause (PENH), with conventional respiratory mechanics measurements. Resistance (RL), dynamic compliance (Cdyn) and pleural pressure changes were measured in six healthy anaesthetised Beagle dogs using a pneumotachograph and oesophageal balloon technique consecutive to BWBP-derived variables. Upper airway airflow limitation was established (1) by a filter or (2) by insertion of a narrow endotracheal tube. Bronchoconstriction was induced by nebulisation of carbachol at increasing concentrations until PENH exceeded 300% baseline.

Upper airway narrowing significantly increased resistance (baseline RL 2.0 ± 0.3, RL filter 11.8 ± 3.2, RL luminal narrowing 21.1 ± 2.3 cm H_2O/L/s; $P < 0.03$), whereas PENH did not change significantly (baseline PENH 0.55 ± 0.17, PENH filter 0.49 ± 0.10; PENH luminal narrowing 0.50 ± 0.18; $P > 0.05$). Carbachol-induced bronchoconstriction caused a significant increase in PENH (baseline PENH 0.43 ± 0.14, PENH carbachol 2.62 ± 2.14; $P < 0.02$) and resistance (baseline RL 2.1 ± 0.3, RL carbachol 28.8 ± 13.0 cm H_2O/L/s; $P < 0.01$), and a pronounced drop in compliance (baseline Cdyn 163.3 ± 73.9, Cdyn carbachol 9.7 ± 2.9 mL/cm H_2O; $P < 0.02$). It was concluded that BWBP detects airflow limitation due to bronchoconstriction but not due to upper airway obstruction in healthy dogs. BWBP represents a valid, although not very sensitive screening tool for respiratory function testing.

Keywords: Canine; Pulmonary function testing; Enhanced pause (PENH); Barometric whole body plethysmography (BWBP); Carbachol

Introduction

Single chamber barometric whole body plethysmography (BWBP) has been used for decades in rodent models of respiratory disease in order to evaluate airway responses to agonists of airflow limitation and to assess the effects of antagonistic drugs. Since the technique is non-invasive and can be performed repeatedly in the same conscious, unrestrained animal, there has been considerable interest in applying it to other species and in veterinary clinical patients.

Several reports have been published in recent years on the application of single chamber BWBP in cats (Hoffman et al., 1999; Hirt et al., 2003; Kirschvink et al., 2005a), dogs (Hirt et al., 2005; Talavera et al., 2006) and pigs (Halloy et al., 2004), describing detection of spontaneous or induced airflow limitation, reversal or prevention of airflow limitation by bronchodilators, and airway responsiveness testing. A surrogate parameter for airflow limitation can

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be obtained from BWBP signals by calculating the enhanced pause (PENH). By performing airway challenges with agonists of airflow limitation and establishing dose–response or concentration–response curves, it is possible to detect airway hyper-responsiveness, which is a well known phenomenon in inflammatory small airway disease (Sears et al., 1986; Tashkin et al., 1992; Theodorou et al., 1997; Van Schoor et al., 2000).

A key feature of airway hyper-responsiveness is the occurrence of airflow limitation after inhalation of low agonist levels, when compared to healthy individuals. Although PENH cannot be used as a direct substitute for resistance (measured with conventional methods) under all respiratory conditions, it does describe and reflect the effort exerted on the expiratory phase of breathing after administration of (pharmacological) stimuli that are known to induce airflow limitation, and may therefore serve as a surrogate for more classical measurements of airway obstruction (Chand et al., 1993; Hamelmann et al., 1997).

The application of BWBP as a pulmonary function test, and especially the use of PENH as a parameter to detect and quantify increased airway resistance in mice, rats and guinea pigs, has been severely criticised by some investigators (Enhorning et al., 1998; Lundblad et al., 2002; Adler et al., 2004; Bates et al., 2004). The main criticisms arise from the lack of validation of the method for different animal species under varying conditions and from the fact that PENH is not a direct parameter of the mechanics of breathing. Nevertheless, BWBP with PENH measurement is still considered a suitable screening tool for the diagnosis of lower airway disease in cats, (Hoffman et al., 1999; Hirt et al., 2003; Rozanski and Hoffman, 2004; Kirschvink et al., 2005b), swine (Halloy et al., 2004) and dogs (Hirt et al., 2005; Talavera et al., 2006).

The purpose of the present study was to investigate the suitability of BWBP and PENH against a reference method measuring direct parameters of respiratory mechanics, namely resistance (RL), dynamic compliance (Cdyn) and maximal pleural pressure changes (dPmax), in healthy anaesthetised, spontaneously breathing dogs undergoing (1) artificial upper airway obstruction, and (2) airway responsiveness (bronchoprovocation) testing with cholinergics, and to further illuminate the relationship between PENH and RL and Cdyn. To the authors' knowledge, this is the first report in healthy dogs comparing BWBP with a reference method under different airway conditions (agonist-provoked airflow limitation, induced upper airway obstruction).

Materials and methods

Animals

The study was conducted in six clinically healthy castrated male Beagle dogs (median age 1.9 years, range 1.8–2.0 years). Bodyweight ranged from 16 to 19 kg. None of the dogs had a history or clinical signs consistent with respiratory tract disease prior to the study. The overall health and respiratory tract status of the animals were assessed by physical examination, complete blood count, biochemical blood analysis, faecal examination, thoracic radiographs, arterial blood gas analysis, bronchoscopy and bronchoalveolar lavage (BAL) fluid analysis (quantitative nucleated cell counts, cytology and microbial culture).

All experimental procedures were approved by the Austrian Ministry of Health and the Veterinary University of Vienna Animal Welfare Commission.

Procedures

Respiratory mechanics

For the measurement of RL, Cdyn, dPmax and PENH, the dogs were anaesthetised with pentobarbital (10 mg/kg IV) 20 min after pre-medication with acepromazine (0.03 mg/kg IV) and buprenorphine (0.01 mg/kg IV). Dogs were positioned in lateral recumbency in the BWBP box (see below), and care was taken that the angle between head and neck remained >45° in order to avoid tracheal flexion throughout the procedures.

A 9 mm internal diameter (ID) endotracheal tube (ETT) was placed in each dog's trachea with the cuff inflated and the outer end of the tube connected to a pneumotachograph (size 1, Fleisch) at the time of measurement. The pneumotachograph was connected to a differential pressure transducer (DP 45-14, Validyne Engineering) by two equally long tubes with 4 mm ID. An oesophageal balloon catheter (balloon length 5 cm) was placed in the thoracic oesophagus at a position where pressure variations reached their maximum (mid to lower third), and connected to a differential pressure transducer (DP 45-28, Validyne Engineering) for recording pressure changes as a surrogate for intrapleural pressure. Volume calibration was performed using a 100 mL syringe, whereas for pressure calibration a water manometer was used.

Downstream, the transduced signals were amplified using a strain gauge amplifier (Buxco Electronics Inc.), which was digitised and sampled. Analysis of the waveforms on a breath-by-breath basis was performed using commercial software (Buxco XA Biosystem, Anesthetized Animal Measurements, Traditional Mechanics). From simultaneous airflow and oesophageal pressure measurements, RL, Cdyn and dPmax were calculated by the software. For the ease of repeated measurements of BWBP derived parameters and respiratory mechanics, the electrical cords of the differential pressure transducers for the respiratory mechanics setup exited the BWBP box through a sealed opening in one of the walls.

Barometric whole body plethysmography

Data acquisition of BWBP-derived respiratory parameters were performed using minor modifications of the method that has already been described for cats (Hoffman et al., 1999). Briefly, the dogs were placed in a non-compliant polymerised methyl methacrylate box (inner volume175 L) that was sealed with a lid for BWBP measurements. On one wall of the main chamber was placed a screen serving as low-pass filter, thereby permitting dynamic assessment of box pressure fluctuations. One pole of an ultra low-pressure differential transducer (±10 cm H_2O, SCXL004, Invensys Sensor Systems) was open to the main chamber, and the other pole to a reference compartment mounted on one wall of the main chamber. The reference chamber communicated with the atmosphere through a low-pass opening (1.5 mm diameter hole, 67% decrease in pressure over 10 s).

A continuous bias flow of 5 L/min was employed to maintain oxygen levels and prevent carbon dioxide from accumulating in the chamber. In addition, after nebulisation of each concentration of cholinergic agonist into the box and consecutive measurement of BWBP derived parameters, the lid was opened to enable connection of the pneumotachograph to the outer end of the endotracheal tube for measurement of classic respiratory mechanics. This also allowed for normalisation of box temperature, humidity and gas composition. Downstream, the transduced signals were amplified using a strain gauge amplifier (Buxco Electronics Inc.), digitised and sampled. Analysis of the waveforms on a breath-by-breath basis was