Journal of Cystic Fibrosis 13 (2014) 190 – 197

Journal of Cystic Fibrosis

www.elsevier.com/locate/jcf

Original Article

Impact of different breathing protocols on multiple-breath washout outcomes in children

Sophie Yammine [a,b], Florian Singer [a,c], Per Gustafsson [d], Philipp Latzin [a,b,*]

[a] Division of Respiratory Medicine, Department of Pediatrics, University Children's Hospital of Bern, Switzerland
[b] University Children's Hospital of Basel UKBB, Switzerland
[c] University Children's Hospital of Zurich, Switzerland
[d] Department of Pediatrics, Central Hospital, Skoevde, Sweden

Received 3 June 2013; received in revised form 26 August 2013; accepted 29 August 2013
Available online 25 September 2013

Abstract

Background: To standardize multiple-breath washout (MBW) measurements, 1 L tidal volume (V_T) protocols were suggested. The effect on MBW derived ventilation inhomogeneity (VI) indices is unclear.
Methods: We compared VI indices from free breathing MBW at baseline to 1 L V_T MBW performed in triplicates in 35 children (20 with CF). Mean (range) age was 12.8 (7.0–16.7) years, weight 42 (20–64) kg and height 151 (117–170) cm.
Results: Baseline lung clearance index (LCI) increased from mean (SD) 11.0 (2.2) to 13.0 (2.6), p = 0.011, in CF and from 6.8 (0.5) to 7.7 (1.4), p = 0.004, in controls. Moment ratio and Scond similarly increased. While change in VI indices was heterogeneous in individuals, decrease in functional residual capacity was most strongly associated with LCI increase.
Conclusion: MBW protocols strongly influence measures of VI. The 1 L V_T MBW protocol leads to overestimation of VI and is not recommended in children.
© 2013 European Cystic Fibrosis Society. Published by Elsevier B.V. All rights reserved.

Keywords: Children; Cystic fibrosis; Respiratory function test; Lung physiology; Clinical use

1. Introduction

Multiple breath washout measurement (MBW) has gained wide acceptance as a sensitive test to assess small airway disease such as in cystic fibrosis (CF) [1–3]. MBW can easily be performed in all ages including children [4–7]. The most commonly reported MBW outcome is the lung clearance index (LCI), a measure for overall ventilation inhomogeneity (VI) [4]. Additional markers, which are considered to be specific for the lung region wherein VI arises, are derived from slope analysis of the alveolar phase III (SIII) of the expired tracer gas. The two most frequently reported SIII-derived indices are referred to as Sacin, for VI occurring near the acinar entrance and Scond, for VI generated in the more proximal conductive lung zone [8,9].

Measures of overall and specific VI, however, largely depend on the size of lung volumes [10–12]. Fixed breathing protocol at one liter tidal volume (1 L V_T) was introduced many years ago [8,9] to ensure sufficient SIII for Sacin and Scond analysis and to improve comparability of VI indices between subjects breathing at different tidal volumes. This breathing protocol is widely used in adults and adolescents [9,13,14]. Different approaches are used in children, varying from entirely free tidal breathing, using an incentive with a given V_T of 10–15 mL/kg [15] to fixed protocols using 0.5 L in younger and 1 L in older subjects or even augmented breaths in infants [16]. The latest ERS/ATS consensus is that breathing protocols of 1 L V_T may not be feasible in all age groups with a suggested cut-off of >16 years, but evidence is lacking [15]. The impact of different breathing protocols on VI indices in children is unclear.

* Corresponding author at: University Children’s Hospital UKBB, Spitalstrasse 33, 1 Postfach, 4031 Basel, Switzerland. Tel.: +41 61 704 19 11.
E-mail address: philipp.latzin@ukbb.ch (P. Latzin).

1569-1993/$ -see front matter © 2013 European Cystic Fibrosis Society. Published by Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.jcf.2013.08.010

We thus compared nitrogen (N_2) MBW results of the most frequently used adult protocol (1 L V_T) with the most frequently used pediatric protocol (free tidal breathing) in school children of a wide age range. Primary outcome was change in LCI at 1 L V_T compared to free tidal breathing, defined as baseline. Secondary outcomes were changes in other parameters of VI and to characterize the physiological mechanisms for the observed change in LCI/VI.

2. Methods

2.1. Study design

In this prospective cross-sectional study 15 children with CF and 20 healthy children aged between 7 and 17 years were enrolled between January and July 2012 at the Children's University Hospital of Bern. We recruited children with confirmed CF attending the outpatient clinic and age-matched healthy controls from local schools and playgroups.

The study was approved by the Ethics Committee of the Canton of Bern, Switzerland. The children's assent was obtained and parents or caregivers provided written informed consent.

2.2. Nitrogen multiple breath washout measurement

We used a recently validated N_2MBW setup as described previously (Exhalyzer D and Spiroware, Eco Medics AG, Duernten, Switzerland) [17,18]. All children performed 6 technically acceptable N_2MBW tests: 3 baseline N_2MBW at entirely free tidal breathing without an incentive, followed by 3 N_2MBW with expired V_T aiming to be between 0.95 L and 1.4 L according to current guidelines for the 1 L V_T protocol [15]. For this, a visual volume-driven incentive was used aiming at 1 L inspiratory volume. Children performed N_2MBW while sitting upright, wearing a nose clip and breathing through a snorkel mouth piece. Maximal in- and expiratory flows monitored online had to be <1 L/s during the entire measurement. N_2MBW was stopped after three breaths below 1/40th of N_2 starting concentration. Baseline N_2MBW runs were accepted if functional residual capacity (FRC) varied less than 20% [19]. N_2MBW outcomes were LCI, FRC, moment ratio (MR = M2M0), Sacin and Scond, number of washout breaths (Nr of breaths), airway deadspace (V_D) and in- and expiratory flows. In addition we calculated the coefficient of variation of V_T (CV_{VT}) as a measure of variability of tidal breathing.

2.3. Nitrogen multiple breath washout analysis

All washout data were recorded and analyzed using Spiroware 3.1.6 (Eco Medics AG). All outcomes were calculated as currently recommended [15]. LCI was calculated as cumulative expired volume (CEV) divided by FRC [20]. FRC was calculated as the ratio of exhaled net N_2 volume to the difference in starting and ending end-tidal N_2 concentration values. The phase III plateau for calculation of SIII-derived Scond and Sacin was determined automatically between 65 and 95% of expired volume after visual control of sufficient phase III and exclusion of phase IV if present. For Scond and Sacin calculation, SIII was normalized for mean N_2 concentration over the interval used for SIII calculation (SnIII) and corrected for V_T (SnIII * V_T) [21]. Airway V_D was calculated by a software using Fowler's method on the CO_2 expirogram [22]. The CV_{VT} was calculated as the percentage of standard deviation divided by the mean of V_T. Additionally the ratio of V_T/FRC was calculated.

2.4. Statistical methods

Our estimate of the sample size was based on published baseline LCI values for a population of school-aged children in Switzerland using the same equipment, with mean ± SD LCI of 6.1 ± 0.9 for healthy children [18]. To detect a minimum difference of one SD LCI from the two N_2MBW protocols with a power of 80% at a two sided 5% significance level, 16 children would be needed to complete the study. Based on an estimated failure rate of 20% [3,4], we aimed to recruit 20 children. Mean value of the 3 baseline N_2MBW and of the 3 N_2MBW tests at 1 L V_T were used for analysis.

Change in LCI (Δ LCI) between 1 L V_T and baseline was the primary outcome. Further indices derived from N_2MBW (MR, Scond, Sacin, FRC, CEV, CV_{VT}, V_T/FRC, Nr of breaths, V_D, in- and expiratory flows) were compared between protocols by paired *t*-test.

Secondly, Δ LCI was related to what could be expected solely due to between-test variability of LCI. Children were stratified into two groups according to their Δ LCI, with natural variability of 12% as cut-off based on a previous study [18]. Age, weight and N_2MBW indices were compared between the two groups by unpaired *t*-test.

In a last step we assessed which variable may determine Δ LCI or Δ MR by uni- and multivariable regression models. The following variables were entered separately into the model: baseline LCI, baseline FRC, Δ FRC, Δ V_T, Δ CV_{VT}, Δ V_T/FRC, Δ Nr of breaths and Δ V_D. If no linear association was present, variables were grouped according to the best fit of the model. We then used a backward stepwise exclusion strategy to obtain a final model of all variables that were significantly associated with Δ LCI or Δ MR respectively (cut off p-value <0.1). All analyses were done using Stata™ (Stata Statistical Software: release 11. College Station, TX: StataCorp LP).

3. Results

We studied 20 healthy children (7 boys), aged mean (range) 13.0 (7.8–15.9) years and 15 children with CF (4 boys), aged 12.4 (7.0–16.7) years. Mean (range) weight and height were 45 (27–64) kg, 154 (128–170) cm in healthy children and 40 (20–60) kg, 147 (117–169) cm in children with CF. There was no statistical significant difference for age, weight or height between groups. All children were able to adhere to both protocols, performing 3 N_2MBW at free tidal breathing and 3 at fixed breathing with $V_T \geq 1$ L by significantly increasing their V_T (Table 1) and V_T/kg respectively. In three children with CF two instead of three

Download English Version:

https://daneshyari.com/en/article/6240883

Download Persian Version:

https://daneshyari.com/article/6240883

Daneshyari.com