Should ventilator target tidal volumes be adjusted for gestational age?

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Background: Preterm infants are susceptible to volutrauma, but lung volumes and capacities may vary. The relationship between gestation and the alveolar deadspace and tidal volumes is unknown.
Aims: To measure $V_{d,MM}$ on day 1 of life in ventilated very preterm infants. We hypothesized that after adjusting for set target tidal volume on the ventilator ('volume guarantee') and respiratory rate, the ratio of alveolar to total tidal volume (V_{alv}/V_T) increases with gestational age at birth.
Methods: 120 s of tidal breathing were recorded from unsedated, sleeping preterm infants (n=43; gestation 23-31 w, mean (SD) birth weight 1.1 (0.4) kg, postnatal age 14.3 (7.2) h) receiving patient-triggered ventilation (Babylog 8000 plus, Draeger Medical, Luebeck, Germany) using a mainstream ultrasonic flowmeter (Spiroson Exhalyzer D, Ecomedics AG, CH). Airway deadspace was calculated from the molar mass signal ($V_{d,MM}$). Alveolar volume (V_{alv}) was calculated as $V_T - V_{d,MM}$. Arterial blood gases were obtained immediately after lung function testing. Multiple linear regression was used to analyse outcomes.
Results: Mean (SD) values for $V_{d,MM}$, V_T, and V_{alv}/V_T were 2.51 (0.61) mL/kg, 6.57 (1.54) mL/kg, and 0.62 (0.06) respectively. Mean (SD) arterial $PaCO_2$ was 42.9 (5.8) mmHg. V_{alv}/V_T was positively associated with gestational age ($R^2 = 0.26$, $p = 0.012$) after adjusting for set volume guarantee (range 3.8-5.1 mL/kg) and respiratory rate.
Conclusions: In ventilated very preterm infants, V_{alv}/V_T on day 1 increases with gestational age. Ventilator target tidal volumes should be adjusted for maturity as well as body size at birth to avoid potential alveolar overdistension.

Monitoring of young children with CF

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Introduction
Close monitoring of CF patients is necessary. For children aged 0-4 years, currently used lung function tests are cumbersome or not possible. It is important to develop alternative methods to assess pulmonary disease.
Lung Clearance Index (LCI), nightly oxygen saturation (SpO_2), and/or cough audiometry might be valuable tools in the monitoring of these patients.
Aim
To compare LCI, overnight SpO_2 and cough in CF patients aged 0-4 years old with a group of healthy controls.
Methods
Prospective cross sectional study. Children with CF were recruited from the outpatient clinic, healthy children from child day care facilities. We aim to include 20 CF patients and 30 healthy children by April 2010.
Gas mixing was measured by the Exhalyzer®D at the outpatient clinic. Overnight SpO_2 was measured by the Novametrix Model 2001 MARS pulse oximeter and nightly cough was measured with an audiometer. Both were measured at home during a normal night sleep.
Results
To date, 47 subjects were included in this study: 20 CF patients (mean age 2.6 yrs) and 27 healthy children (mean age 2.8 yrs). In this abstract we report preliminary data. Age, sex, height and weight were not significantly different between both groups. Success rate for LCI in these young children was 60%. LCI was higher in CF patients than in healthy controls: mean LCI was 8.02 in the CF group and 6.89 in the control group ($p=0.013$). overnight SpO_2 was 97.53 in healthy children and 96.62 in CF patients ($p = 0.056$). For cough no significant differences were found in this preliminary analysis.
Conclusions
LCI showed a significant difference between healthy children and CF patients at a young age. This suggests that the LCI is the most sensitive test to detect pulmonary changes at an early stage.

Lung clearance index (LCI) and nutritional parameters in infants with cystic fibrosis

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Multiple breath washout (MBW) can be easily performed during tidal breathing in infants. In addition to FRC, indices of ventilation inhomogeneity like the Lung Clearance Index and Moment Ratios (MR1, MR2) can be estimated. We hypothesized that ventilatory indices in infants with CF correlate with their nutritional indices. MBW was performed with 4% Sulfur Hexafluoride and using an Exhalyzer®D (Eco Medics AG, Switzerland). Nutritional status was assessed by weight for age (WAP) and weight for length percentiles (WLP).
Fifteen infants with CF, mean age 16 months (range 3 to 32 months) completed the test without difficulty. The mean (SD) LCI observed in this group was 8.6 ± 1.4 (upper limit of normal 7.1). Mean MR1 was 2.784 ± 0.52 and MR2 14.52 ± 6.28, values that are higher compared to the reported values in healthy infants. Mean WAP was 39.2 (SD26.6), mean HAP was 42 (SD 28) and mean WLP was 57.94 (SD 29.93), reflecting adequate nutrition for the group.There was a correlation between LCI and weight for age percentile (r=0.46), with infants having the lowest WAP having the highest LCI. Similarly, there was a correlation between LCI and WLP(r= 0.51), infants with a lower WLP having the highest LCI. No other correlations were found between pulmonary function parameters and nutritional indices. We found a relationship between malnutrition and lung clearance index in this group of infants with CF. This can be taken as additional evidence for the strong influence of nutritional status and lung disease early in life. In addition, MBW measurements have an excellent potential as clinical endpoints in infants with CF.

Impaired weight gain in CDH infants hampers the analysis of lung development

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Background: Infants with congenital diaphragmatic hernia (CDH) require a prompt surgery, which affects gas exchange, lung mechanics and the postnatal lung development. The aim of the study was to investigate the relationship between the post-operative lung function and the lung function at one year of life.
Methods: In 7 newborns with CDH (mean weight 2695±556g at surgery) respiratory compliance (C_{resp}) and functional residual capacity (FRC) were measured during mechanical ventilation before surgery and at extubation (heptafluoropropane multiple breath washout (FRC_{HFP}), Babylog 8000, Dräger). At the age of one year (12.1±1.1month, body weight 8096±1598g) a lung function testing was performed (Jaeger Babybody (FRC_{Pleth}) and ECO MEDICS Exhalyzer D (FRC_{SF6})).
Results: Before and after CDH surgery C_{resp} was not changed (2.5±1.0 vs. 2.9±0. 9mL/kPa/kg; p=0.167), while FRC_{HFP} increased distinctly (8.99±2.07 vs. 13.7±3.61 mL/kg; p=0.003). Nevertheless, despite this improvement, the lung function remained significantly impaired. At one year of life C_{resp} was 13.1±2.9mL/kPa/kg, FRC_{Pleth} was 27.6±7.4mL/kg and FRC_{SF6} was 26.3±6.2mL/kg, which are close to or above published reference values. There was a strong correlation between the post-operative lung volume and the weight gain during the first year of life (r=0.935, p=0.02). The lower the post-operative lung volume the lower was the weight gain suggesting an overestimation of C_{resp} and FRC if related to body weight at 1 year of life.
Conclusions: Depending on the post-operative lung function CDH infants have an impaired weight gain during the first year of life which hampers the interpretation of weight related lung function parameters.

Single breath washout of double tracer gas in children with and without cystic fibrosis

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Ventilation inhomogeneity (VI) can be assessed by multiple breath washout (MBW), however this test requires cooperation and time. We assessed whether a modified single breath washout (SBW) test using double tracer gas (DTG) is feasible in children, and provides information on VI in CF lung disease.

26 (16 males) children with stable CF lung disease, mean age 11.9 (SD 3.9) years, and 13 (8 males) healthy children, mean age 12.7 (6.3) years, performed MBW and SBW tests. Molar mass (MM) was measured with a side stream ultrasonic flow meter (EcoMedics AG). DTG mixture contained helium (He) and sulfur hexafluoride (SF6) with a similar MM as air. During tidal breathing, air was switched to DTG for one inspiration. The shape of the DTG washout curve was expressed as a SF6/He ratio against expired volume.

Three tests of SBW took less than five minutes and were feasible in all children. Visual analysis revealed three categories based on SF6/He slope, and overall and end-tidal SF6/He. The ratio of healthy to CF children was 0:16 in group I, 6:8 in group II and 7:2 in group III. Mathematical analysis showed significant differences between healthy and CF children for several parameters, e.g. mean (95%-CI) area under the SF6/He curve was 188 (152 – 224) for healthy and 105 (51 – 159) mg*l/mol for CF subjects ($p=0.011$). Relative rate of change in SF6 washout was strongly correlated with lung clearance index ($r=0.624$; $p<0.001$).

Tidal SBW is fast and easy to perform, and seems to provide a good measure of overall VI. Furthermore, detailed analysis of the DTG washout curve may provide additional and yet unknown information on VI, possibly of interest in children with CF.

Is lung clearance index a better marker of abnormal airway function than FEV_1 in children with asthma?

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Introduction

Traditional lung function measures such as forced expiratory volume in 1 second (FEV_1) are of little value in classifying asthma severity in children [Bacharier, AMJRCCM 2004]. We hypothesized that lung clearance index (LCI) a measure of ventilation heterogeneity derived from multiple breath inert gas (SF6) washout measurements may be a more sensitive marker of airways disease than FEV_1.

Methods

Children with asthma (n=20, median age 8.8 years) and controls without respiratory symptoms (n=13, median age 8.2 years) underwent triplicate multiple breath washout of SF6 and spirometry on the same occasion. They were further divided into severe asthmatics (persistent symptoms despite treatment with ≥ 800mcg of inhaled budesonide or equivalent per day (n=14)) and mild-moderate asthmatics (symptoms controlled on steps 1-3 of British Thoracic Society guidelines (n=6)). None had an acute exacerbation at the time of investigation. LCI of ≥ 7.2 was considered raised [Gustafsson, Thorax 2008].

Results

Severe asthmatics had higher LCI (median 7.8 [range 6.1-11]) when compared with age matched controls (median 7.2 [range 6.2-7.6]) (p=0.037). There was no difference between mild-moderate (median LCI 7.4 [range 6.6-8.9]) and severe asthmatics or controls. No difference in FEV_1 was detected between the 3 groups (p=0.35). Eight asthmatic children with normal FEV_1 (≥80%) had an increased LCI.

Conclusion

LCI is a more discriminative test in assessing airway function in asthmatic children, and may be a particularly useful tool in assessing asthmatics with normal FEV_1.

Effect of airway deadspace calculation method on lung clearance index in preterm infants

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Background: Airway deadspace (V_d), calculated from the molar mass signal ($V_{d,MM}$) of an ultrasonic flowmeter (USF) shows good agreement with Fowler deadspace in infants.
Aims: To assess whether $V_{d,MM}$ differs from V_d estimated by body size ($V_{d,BS}$) or gas dilution factor ($V_{d,DF}$) derived from multiple breath washout (MBW) in preterm infants. We hypothesized that a) $V_{d,MM}$ is smaller than $V_{d,BS}$ and $V_{d,DF}$, b) presence of chronic lung disease (CLD) alters these differences in V_d, and c) the impact of V_d to tidal volume ratio (V_d/V_T) on lung clearance index (LCI) depends on the method of calculating V_d.
Methods: Thirty-seven preterm (gestational age 23 – 33 w, CLD: n=16) and 19 term healthy infants were studied in quiet sedated sleep using an USF at 15-18 m corrected age. $V_{d,MM}$, V_T, and respiratory rate (RR) were calculated during 30 s of tidal breathing prior to MBW with 5% sulphur hexafluoride. Functional residual capacity (FRC), LCI, and $V_{d,DF}$ were calculated from the washout trace. ANOVA and multiple linear regression were used to analyse outcomes.
Results: Mean (SD) $V_{d,MM}$ was smaller than both $V_{d,BS}$ and $V_{d,DF}$: ($V_{d,MM}$ 1.8 (0.74) mL/kg, $V_{d,BS}$ 3.5 (0.24) mL/kg, $V_{d,DF}$ 4.1 (0.74) mL/kg; $p<0.001$). CLD status did not significantly influence these differences. There was no association between CLD and V_d/V_T using any method of calculating V_d. After adjusting for V_T/FRC and RR, LCI was positively associated with $V_{d,MM}/V_T$ ($p=0.005$) and $V_{d,DF}/V_T$ ($p<0.001$). The predictive value of V_T/FRC, RR, and V_d/V_T on LCI varied with the method of calculating V_d.
Conclusions: Standardised correction for deadspace is necessary in the assessment of LCI to ensure valid comparisons in preterm infants.