

European Respiratory Society Annual Congress 2013

Abstract Number: 3871

Publication Number: P1102

Abstract Group: 7.1. Paediatric Respiratory Physiology

Keyword 1: Interstitial lung disease **Keyword 2:** Children **Keyword 3:** Physiological diagnostic services

Title: Comparison of carbon monoxide diffusion using breath hold and rebreathing techniques in children with interstitial disease

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Body: Background Carbon monoxide diffusion (DLCO) measured with reabreathing (RB) technique and hyperventilation has been found to equal breath holding (BH) measure in healthy adults using homemade device. No assessment of the commercially available RB machine has been performed in sick children in whom BH technique might be difficult to achieve. Objectives 1) to assess feasibility and repeatability of DLCO_{RB} 2) to compare DLCO_{BH} and DLCO_{RB} in sick children. Methods Prospective monocentre study in 46 children with suspicion or actual interstitial disease, able to perform DLCO_{BH}. DLCO_{BH} and RB were measured in duplicate (Masterscreen, Jaeger, Hoechberg, Germany). Results Correct DLCO_{RB} measurements during tidal breathing was obtained in 41 (89%) children (age median 11.8 [8.2 to 18.2]y). Median (IQR) z-score of DLCO_{AP} was -1.94 (-3.30;-1.84)[-9.9 to 1.37]. Functional residual capacity of the two DLCO_{RB} measurements was reproducible (within 15%). Alveolar volume (VA) of DLCO_{RB} was lower to that of DLCO_{BH} (VARB median 52.6 [41.9 to 75.1]% of VABH). The duplicated measurements of DLCO_{RB} and DLCO_{BH} were within 15% in 76% and 95% of the children, respectively. DLCO_{RB} and DLCO_{BH} were highly correlated ($r^2 = 0.72$, $p < 0.0001$) even though DLCO_{RB} was lower than DLCO_{BH} (median 3.26 vs 4.88 mMol/kPa/min; $p < 0.0001$; DLCO_{RB} -33.5 [-58.3 to 23.6]% of DLCO_{BH}). Conclusion DLCO_{RB} technique is feasible (89%) and reproducible (76%) in children able to perform BH technique despite various level of interstitial impairment. DLCO_{RB} is highly correlated to DLCO_{AP}. Further studies to determine reference values and measurement in younger children are warranted before using RB technique in routine.