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Title: Long-term reproducibility of exhaled nitric oxide and exhaled breath temperature in healthy children

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Body: Background Measurements of the fractional concentration of exhaled nitric oxide (FE_{NO}) and exhaled breath temperature (EBT) are easy to perform, non-invasive and considered reproducible at short-term; data on their long term reproducibility is needed. Aims To assess reproducibility of FE_{NO} and EBT in healthy children one-year apart and their relationship with lung function and anthropometric changes. Methods In 41 healthy children (24 males) aged 9.8 ± 1.6 yr, range 8.0-13.8, we obtained duplicated measurements of FE_{NO} and EBT in two sessions one-year apart (2011 and 2012). Subjects did also spirometry in both sessions. The intraclass coefficient correlation (ICC) and the coefficient of repeatability (CR=2 SD) were assessed. Overtime changes in variables ("D" prefix) were calculated. Results Intra-session reproducibility of duplicate measurements was high in both sessions [(ICC >0.94 for both FE_{NO} and EBT); (CR: FE_{NO} 5.2 ppb and 3.0 ppb, EBT 1.8 and 1.2 °C)]. Geometric means (95% confidence interval) did not change significantly from the 2011 to the 2012 sessions [FE_{NO} : 10.6 (9.3-12.2) ppb and 10.2 (9.2-11.3) ppb; EBT: 32 (31.3-32.7) °C and 32.6 (31.9-33.2) °C]. Reproducibility decreased after 1 year [FE_{NO} (ICC: 0.48, CR: 11.0 ppb); EBT (ICC: 0.75, CR: 3.5 °C)]. The between-year percent increase in FE_{NO} correlated with decreased lung function ($DFEV_1\%$ $r=-0.33$, $DFEF_{25-75}\%$ $r=-0.39$, $p<0.05$) whereas EBT increased with BMI (DBMI 0.41, $p=0.008$). Conclusion Reproducibility of both FE_{NO} and EBT decreases after one year in healthy children; their changes have a different meaning; FE_{NO} is more affected by changes in bronchial patency whereas EBT by increases in body mass index.