



Effect of change of body position in spontaneous sleeping healthy infants on SF₆-based multiple breath washout

To the Editor:

Reference values previously published in the *European Respiratory Journal* for sulfur hexafluoride (SF₆)-based multiple breath washout (MBW) [1] highlight that lung clearance index (LCI) values were significantly higher in infancy (*i.e.* first two years of life) compared with the later preschool age range (2–6 years). A number of factors were postulated in recent American Thoracic Society (ATS) preschool MBW technical standards [2]: ongoing lung and chest wall development [3]; use of sedation and supine testing position in infancy; and relatively larger equipment-related dead space volume (V_D) in younger subjects. Use of alveolar-based LCI to correct for V_D did not change this pattern suggesting minimal V_D impact as a mechanism to explain these changes [4]. Specific to body position, infants are tested supine (as asleep) and preschoolers are tested sat upright (as awake). The impact of changing body position remains unclear on MBW outcomes. Our aim was to investigate effect of body position on ventilation distribution, resting lung volume (functional residual capacity; FRC) and breathing pattern in healthy infants during spontaneous sleep.

Parents/caregivers of infants in East Skaraborg County, Sweden, were identified *via* the Swedish population register and sent an information letter ($n=200$). Full-term infants without a history of congenital lung malformations or respiratory health problems other than common transient infections were eligible. We aimed to include a minimum of 40 subjects, over a 12-month period, based on the assumption that for a normally distributed variable we would be adequately powered to detect a difference of 0.5 SD of the within-person differences. The study was approved by the Ethics Committee of the University of Gothenburg (Gothenburg, Sweden; DNR 746–15), and parents gave written informed consent.

The commercial MBW device used (ExhalyzerD, Eco Medics AG, Spiroware 3.2.1, Duernten, Switzerland) had been previously validated by our group for SF₆-based MBW in the infant age range [5]. This open-circuit MBW system measures SF₆ concentrations indirectly *via* recorded signals including main-stream CO₂, side-stream O₂, side-stream molar mass (MM_{ss}), and respiratory flow using a main-stream ultrasonic flow meter (UFM_{ms}). UFM_{ms} calibration using a 100-mL precision syringe (Hans Rudolph, Shawnee, KS, USA) and static calibration of O₂ (air and 100% O₂, respectively) and SF₆ signals (air for zero, and 4.0% SF₆ in air, respectively) with certified test gases (Linde Healthcare, Lidingö, Sweden) were undertaken as per manufacturer's instructions. Dynamic synchronisation of MM_{ss} and gas to respiratory flow was performed during room air breathing separately in all participants [5]. A #1 dead space reducer was used in all recordings. A putty-sealed stiff paediatric face mask Rüsck #1 or #2 (Teleflex Medical, Athlone, Ireland) was used depending on subject's face size. Pre- and post-gas-sampling point dead space volumes were set to 0 mL and 3.5 mL, respectively. Dead space volume of the mask was minimised using therapeutic putty and was measured after the recordings. It was found to vary between individuals across the range of 3–8 mL and was not corrected for, in line with recent recommendations [2].

Prior to MBW, infants were fed and MBW recordings started after a sustained period of quiet sleep. Recordings were first made while sleeping horizontally in an infant pushcart and then whilst sitting seated

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Change of body position from supine to sitting had no effect on FRC and only a minimal effect on MBW indices of ventilation inhomogeneity. Change of body position contributes minimally to the difference observed between infant and preschool LCI values. <http://bit.ly/2MjbYFv>

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upright with the backrest at 70 degrees. Priority was given to supine recordings, which were part of a larger study collecting SF₆ MBW reference values. At least two recordings (but ideally three) of acceptable quality were collected in each body position, *i.e.* recordings without evidence of mask leaks or artefacts such as sighs, irregular or fast breathing or breathing interrupted by swallows [6]. After three acceptable supine recordings, the infant was placed in the sitting position and recordings started after confirming ongoing quiet sleep. A prephase of at least 30 s of stable medical air breathing occurred before administration of 4.0% SF₆ gas mixture *via* the bias flow (SF₆ wash-in). When end-tidal SF₆ concentration had stabilised at 4.0% for approximately half a minute, the bias flow was switched medical air to start SF₆ washout, which continued until end-tidal SF₆ had fallen to below 1/40th of its starting concentration for several breaths [6].

Data were analysed in Spiroware 3.2.1. Raw data tables were exported from the software into Microsoft Excel 2010 (Microsoft Corporation, Redmond, WA, USA) for further statistical evaluation. FRC, LCI, moment ratios and breathing pattern variables were calculated, using Excel templates made by the senior author, as described in previous publications [7–9], and consistent with recommendations of the European Respiratory Society (ERS)/ATS consensus statement [6]. Mean±SD and coefficients of variation (100×SD/mean) were calculated for all variables. Paired t-tests and correlation analyses were made using the Statistica 7 (StatSoft, Tulsa, OK, USA). A p-value <0.05 was regarded as statistically significant.

Among 103 healthy infants tested over a 12-month period, 41 (40%) infants performed at least two acceptable tests in each position and were included in the final analysis. In the remaining 62 out of 103 only supine recordings were obtained (data not reported here). Mean±SD (range) age of included infants was 1.00±0.33 (0.40–1.63) years with 23 female infants. Mean±SD (range) weight and height were 10.2±1.7 (7.3–13.6) kg and 75.3±5.1 (65.0–92.8) cm. SF₆ MBW results are summarised in table 1. All infants contributed three acceptable SF₆ MBWs supine and 35 (85%) out of 41 performed three subsequent sitting MBWs. The remaining six had two acceptable tests in the sitting position. On average FRC did not change with posture. Small but statistically significant differences were seen in LCI and moment ratios (both first and second moments), indicating a slightly better global ventilation efficiency sitting. Measured airway V_D using CO₂ was also lower. Tidal volumes were similar, but respiratory rate and minute ventilation were lower when sitting, resulting in a higher end-tidal CO₂ in that position. Between-subject variation in response to change of position was observed. Sitting FRC was lower in 19 (46%) out of 41 infants by mean±SD (range) 11±11 (0–43) mL and higher in the remaining 22 out of 41 infants by 16±10 (0–36) mL. Sitting LCI was lower in 27 (66%) out of 41 infants by 0.33±0.18 (0.03–0.82) lung turnovers and rose in the remaining 14 subjects by 0.12±0.11 (0.00–0.40) lung turnovers. On univariate regression analyses, response to change in position from supine to sitting was age-dependent: FRC, both as actual (r=0.43, adjusted R² 0.16, p=0.005) and mL·kg⁻¹ (r=0.37, adjusted R² 0.12, p=0.016) and LCI (r=-0.33, adjusted R² 0.08, p=0.036). Percentage change in FRC and LCI correlated (r=-0.57, adjusted R² 0.33, p<0.001). We

TABLE 1 Sulfur hexafluoride multiple breath washout and breathing pattern variables compared supine and sitting in 41 infants

	Supine	Sitting	p-value
Washout time s	33±6	34±7	0.19
Washout breaths n	13.4±2.3	12.9±1.9	0.009
FRC mL	185±47	189±54	0.21
FRC mL·kg ⁻¹ b.w.	18.1±2.9	18.4±3.4	0.39
LCI	6.60±0.41	6.45±0.45	0.001
μ ₁ /μ ₀	1.54±0.10	1.51±0.10	<0.001
μ ₂ /μ ₀	4.46±0.59	4.26±0.59	<0.001
FRC CV%	2.0±1.2	2.0±1.5	0.75
LCI CV%	2.4±1.4	2.8±1.9	0.37
V _{Daw} CO ₂ mL	21±4	20±4	0.003
V _{Daw} CO ₂ /VT %	22±2.6	20.8±2.9	<0.001
V _T mL	96±23	98±22	0.09
V _T /FRC %	53±8	53±7	0.63
Respiratory rate breaths·min ⁻¹	24.3±4.3	22.9±2.9	<0.001
Minute ventilation mL·min ⁻¹	2263±323	2180±296	<0.001
CO ₂ end-tidal %	5.85±0.32	5.92±0.34	0.002

Data are presented as mean±SD, unless otherwise stated. FRC: functional residual capacity; LCI: lung clearance index; V_{Daw}: airway dead space; V_T: tidal volume.

speculate that response to change of position may reflect contributions of several factors influenced by age including active control of FRC, respiratory system mechanical properties (e.g. lung and chest wall compliance) and minor differences in sleep state.

This is the first study to describe how change of position affects measurements of lung volume (FRC) and indices of ventilation inhomogeneity within healthy infants, the specific age group of interest when discussing the impact of positional change on longitudinal MBW measurements. Of note, our reported changes are markedly smaller than that previously reported in older healthy children, where change from supine to sitting led to a mean increase in FRC of 31–40%, and a mean decrease in LCI of 3.4–6.1% [10, 11]. In our cohort of infants, change of body position had no effect on FRC and only a minimal effect on MBW indices of ventilation inhomogeneity (e.g. 2.3% change in LCI). How the age-dependent effect we observed amongst our infants behaves beyond infancy is unclear, but our data highlight the error in extrapolating results from older age groups and reinforces the importance of age-specific data. Our data supports the conclusion that healthy infants do not need to be tested in the seated position to attain a consistent body position with older children: change of body position contributes minimally to the difference observed between infant and preschool SF₆ MBW LCI values. This is an important finding for longitudinal studies both historically and in the future and for understanding the mechanisms of higher LCI values in infancy.

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