Evaluation of the interrupter technique in healthy, unsedated infants

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Evaluation of the interrupter technique in healthy, unsedated infants. G.L. Hall, J.H. Wildhaber, M. Cernelc, U. Frey. ©ERS Journals Ltd 2001.
ABSTRACT: The interrupter technique may be used to monitor respiratory resistance and does not require active patient cooperation, but has yet to be applied in unsedated, spontaneously breathing infants. The aim of this study was to determine if the interrupter technique is feasible in spontaneously breathing infants and to investigate the influence of facemask types and analysis techniques on the interrupter resistance (R_{int}).

R_{int} was measured in 14 healthy, unsedated, sleeping infants (aged 38.4 (31–56) days (mean (range)). Paired measurements were made using large volume, compliant (M_{comp}) and small volume, rigid (M_{rigid}) facemasks. Flow and pressure were measured at the airway opening prior to- and following a brief airway occlusion (500 ms). R_{int} was calculated using four previously reported analysis techniques.

R_{int} could be measured in all infants. M_{comp}, independent of the analysis method significantly underestimated R_{int} (p<0.001). The variability and magnitude of R_{int} were significantly influenced by the choice of analysis method.

The conclusion is that the interrupter technique is feasible in spontaneously breathing, unsedated infants. Equipment design and analysis method significantly influences interrupter resistance. Studies standardizing equipment and identifying the most appropriate analysis technique in this age group are needed.
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The interrupter technique is one of the classical methods for determining the Newtonian resistance of the airway tree. While the technique has some limitations, it only requires minimal patient cooperation hence is of particular interest in young children and infants. There have been a number of recent studies conducted in spontaneously breathing children as young as two years. In particular, the application of this technique to pre-school children has allowed an improved understanding of respiratory disease in this age group [1–4]. The interrupter technique, however, is yet to be standardized and has not been applied to spontaneously breathing infants. The interrupter technique involves rapidly occluding the airway opening and assumes that alveolar pressure (P_{alv}) equilibrates rapidly with airway opening pressure (P_{ao}), following the occlusion, hence allowing the determination of P_{alv}. Following flow interruption of the airway, two distinct phases are seen in the P_{ao} trace. There is an initial rapid rise, followed by a secondary, slower rise to a plateau. The work of BATES and co-workers [5, 6] in animal models has provided a better understanding of the physiological meaning of these changes. The initial rapid rise in P_{ao} reflects the resistive drop across the airway tree and the initial part of the resistive drop across the respiratory tissues, including the chest wall. The slower, secondary change reflects the stress relaxation of the respiratory tissues and to a lesser extent commuting air. The pre-occlusion flow (V') and post-occlusion change in P_{ao} can then be used to calculate the interrupter resistance (R_{int}). P_{ao} following V' interruption is influenced by the closure time of the occlusion valve and the compliance of the upper airways (Cua) [7–9]. The analysis method of the pre- and post-occlusion V' and P_{ao} can also influence the magnitude and variability of R_{int} [2, 10].

Optimal triggering flows (V'_{int}) and occlusion times (t_{int}) may change with differing age groups. Triggering flows, ranging from mid-tidal expiratory flows (0.2–0.4 L·s^{-1}) in adults [10] to peak expiratory flow (0.15–0.2 L·s^{-1}) in five-yr-old children have been reported [2]. In infants, peak expiratory flows (PEF) will be significantly lower than the 0.15–0.2 L·s^{-1} range used in young children and thus V'_{int} of this magnitude would not be suitable. Previously, t_{int} of 100 ms has been most commonly applied, although interruptions of 80 ms have been reported [11]. In infants t_{int} of ≥500 ms are used for the single and multiple occlusion techniques [12].

The aim of the study was to test the feasibility of applying the interrupter technique to spontaneously breathing, unsedated infants. This involved identifying suitable V'_{int} and t_{int}, and investigating the most appropriate face mask type and analysis of the V' and P_{ao} signals.

Methods

Subjects

Fourteen infants (10 males and four females) were studied during quiet sleep, in a supine position with the head in the midline and slightly extended. Infants were aged 38.4 (31–56) days (mean (range)) and had a body weight and length of 4.7 (3.57–5.73) kg and 56.5 (54.0–59.3) cm, respectively. The ethics committee of the University Children′s Hospital of Berne approved the study; the parents gave written consent and were generally present during the study.

Study design

The influence of measurement set-up was studied using two facemasks, one a large volume, compliant walled mask (Mcomp), the other a small volume, rigid walled mask (Mrigid), representing the diversity of masks available. Four previously reported analysis techniques, for the estimation of R_{int}, were employed, utilising the approach of PHAGOO et al. [2, 10, 13–16].

Equipment

Measurements were carried out using commercially available infant respiratory function equipment (Eco-Medics, Duerten, Switzerland). Volume (V), V', and P_{ao} were sampled at 200 Hz with an accuracy of 12 bits. Interruptions were performed with a slide valve (US2000: EcoMedics, Duerten, Switzerland) with a mean closure time of 7.5 ms (range: 6–9 ms). Based on examination of tidal breathing, interruptions were performed at end inspiration at a triggered expiratory flow of 0.020 $L \cdot s^{-1}$, equating to volumes approximating to tidal volume. This flow was chosen to ensure accurate triggering in each infant and to account for the normal variation in end inspiratory flows. Initially, an occlusion time of 100 ms was employed. However upon inspection of the P_{ao} trace (e.g. fig. 1) it was noted that P_{ao} was rapidly increasing at this time point and as such an accurate confirmation of a relaxed passive respiratory system could not be obtained. The occlusion time was subsequently increased to 500 ms, based on the minimum occlusion time recommended for the single occlusion technique, to ensure that a relaxed passive respiratory system
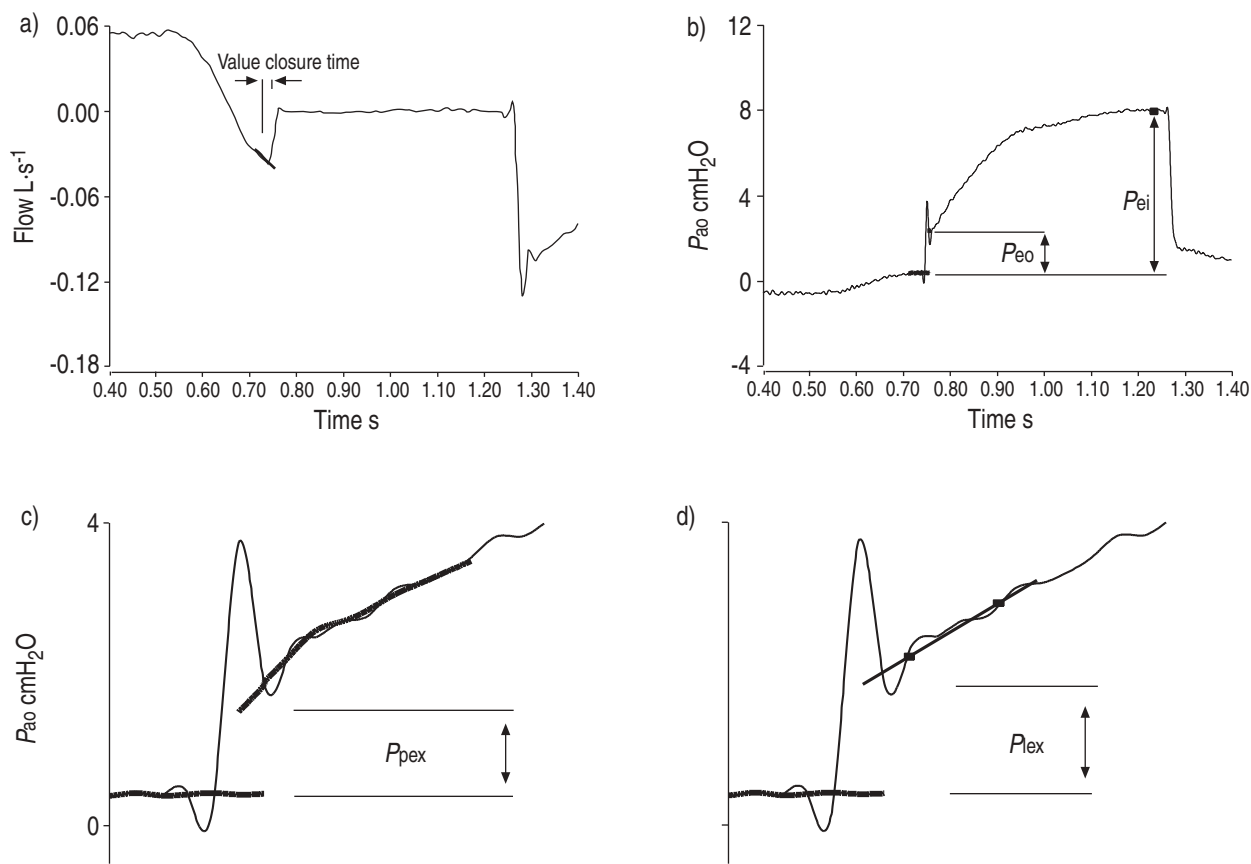

Fig. 1. – a) Representative flow and b) airway opening pressure (P_{ao}) traces following flow interruption in an infant. The interrupter valve was triggered at end inspiration at 20 $mL \cdot s^{-1}$ and held closed for 500 ms. The calculation of the pre-occlusion flow (V') and P_{ao} and post-occlusion P_{ao} values subsequently used to determine interrupter resistance (R_{int}) are also illustrated. The initial rapid rise in P_{ao}, followed by a slower, secondary rise to an end-occlusion plateau can be seen. Pre-occlusion V' and P_{ao} were calculated by extrapolating a smooth polynomial fitting curve to the time of half valve closure (seen in bold lines). Post-occlusion P_{ao} was determined using four previously published methods. c) P_{pex} was determined by back-extrapolating a smooth fitted curve to a time of half valve closure. d) P_{lex} was the instantaneous P_{ao} at half valve closure obtained from a two-point (centred about 30 and 70 ms) linear extrapolation. P_{eo} and P_{ei} were the mean P_{ao} centred about 30 ms and 475–490 ms after half valve closure, respectively.

could be accurately verified [12]. The delay in valve closure due to software and hardware configuration was approximately 40 ms. An ultrasonic flowmeter (M30.8001: EcoMedics, Duerten, Switzerland) was used, and V calculated from the V' signal. Pressure was measured using a piezo transducer (M98.350: EcoMedics, Duerten, Switzerland). The dead space of the flow measurement equipment was determined from its physical dimensions and was 3 mL. The compliant facemask (Mcomp: Size 0, Homedica AG, Cham, Switzerland) had total water displacement volume of 20 mL. The smaller, rigid mask (Mrigid: "Silkomed" Size 1: Model: 852713: Jaeger, Hoechberg, Germany) was lined with putty (REP Putty: Magister, Chattanooga. USA) to ensure a leak free fit and to reduce the dead space, which ranged between 2–5 mL. The total effective dead space of the measurement equipment equated to the sum of the flow measurement dead space and the effective dead space of the mask used (50% of facemask dead space). Hence the equipment dead space was 13 or 4–6 mL for Mcomp and Mrigid, respectively, fulfilling the recently released equipment standards for infant lung function testing [17].

Measurements

Infants were studied during quiet sleep, with the mask placed over the nose and mouth. The tidal flow-volume loops were examined for leak and to ensure that the infant had adjusted to the additional dead space. Once the infant had stabilized, 20 interruptions were performed over a period of approximately 2 min. This number of interruptions was chosen to ensure that a minimum of five acceptable interruptions would be available for analysis. In initial studies it was found that interrupting every three to four breaths allowed relatively constant interruptions to be applied, without disturbing the infant's sleep patterns and maximized the number of interruptions while minimizing the time required. No correlation was found between R_{int} magnitude or variability and the time point at which the interruptions were made. This procedure was carried out initially with Mcomp and then repeated using Mrigid. Following collection, data were stored for off-line analysis. Data were examined prior to analysis and excluded if evidence of leak, breathing or incomplete muscle relaxation were noted as follows: an obvious lack of rise in P_{ao} following interruption, or a rapid decay in P_{ao} during interruption, both indicative of leak around the face mask; obvious sudden decreases or increases in P_{ao} during the interruption period resulting from breathing efforts or incomplete relaxation.

Analysis

R_{int} was calculated by dividing the change in P_{ao} due to the interruption by the flow just prior to the interruption, and may be given as:

$$R_{int} = dP_{ao}/V'_{pre} = (P_{post} - P_{pre})/V'_{pre} \qquad (1)$$

where P_{pre} and V'_{pre} equate to the P_{ao} and V' prior to

interruption and P_{post} is P_{ao} at a given time point following interruption.

V'_{pre} and P_{pre} were calculated by fitting a polynomial curve to the V' and P_{ao} traces from 150 to 10 ms prior to the valve closure, the polynomials were then extrapolated from 10 ms prior to valve closure to the time point when the valve was half closed ($t_{closure}$) [15]. Four analysis techniques were used, all previously reported, to ascertain the magnitude of P_{post} (fig. 1). The first three techniques equate to the resistance across the airway tree (*i.e.* airway resistance), while the fourth technique includes the initial and secondary pressure changes and may be equated to the respiratory system resistance (R_{rs}).

Back extrapolating a fitted smooth curve. A polynomial curve was fitted to the P_{post} data from 30–200 ms after $t_{closure}$ [15]. This polynomial was then extrapolated to $t_{closure}$ to obtain P_{post} and R_{int} determined (R_{pex}).

Linear back extrapolation. A straight line was fitted through two time points, each being the mean of 10 ms of data, centred about 30 and 70 ms following $t_{closure}$ [14]. The line was the extrapolated to $t_{closure}$, P_{post} obtained, and R_{int} calculated (R_{lex}).

End-oscillation pressure. The mean pressure 15–25 ms after $t_{closure}$ was calculated [13]. This was taken to approximate the pressure at the end of the oscillations (P_{eo}) and was used to estimate the interrupter resistance (R_{eo}).

End interruption pressure. The mean pressure at the end of the interruption P_{ei} was obtained (475–490 ms). This pressure includes the initial and secondary pressure changes and the calculated resistance equates to R_{rs} [16].

Statistics

All technically acceptable interruptions were analysed (as detailed above) and the values averaged for each mask separately (mean±SD). Group mean data are expressed as mean±standard error (SEM). The coefficient of variability ($CV = SD \cdot mean^{-1}$) was calculated for each infant and for the group. A two-way analysis of variance (ANOVA) was used to test for the effect of mask type and analysis technique. Pairwise multiple comparisons were carried out using the Student-Newman-Kuels method. The statistical tests used were sufficiently powered to accurately detect significant differences due to the mask or analysis technique (power >0.8).

Results

All infants tolerated the measurements well and were not disturbed during the measurement period from their normal sleep. Measurements were normally completed within a 10 min period following sleep onset. Group PEF ranged 33.1–73.3 mL·s^{-1} (56.3± 10.8 mL·s^{-1}: mean±SD) and the chosen V'_{int} of
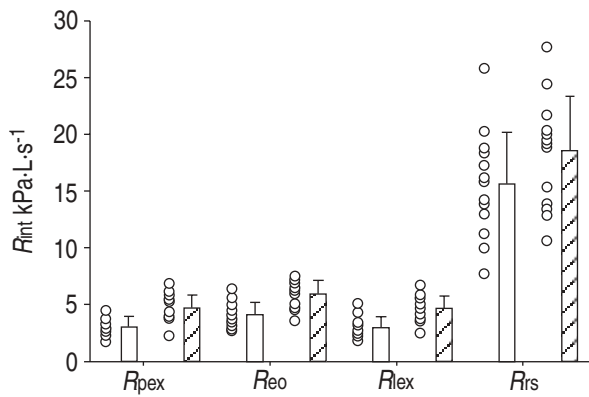
Fig. 2. – Individual (○) and group mean (bars (SD) to right of individual data) interrupter resistance (R_{int}) in healthy, sleeping infants. R_{int} was significantly underestimated if M_{comp} (a compliant, large volume face mask) was used (□: Two way ANOVA; p<0.001), when compared to M_{rigid} (a rigid, small volume face mask) (▨). The analysis technique significantly influenced R_{int} (Two way ANOVA: p<0.001). R_{pex} (R_{int} determined using polynomial back extrapolation method) and R_{lex} (R_{int} determined using linear back extrapolation method) were significantly lower when compared to R_{eo} (instantaneous R_{int} following the end of pressure oscillations) (Pairwise comparison: p<0.05). R_{rs}: respiratory system resistance.
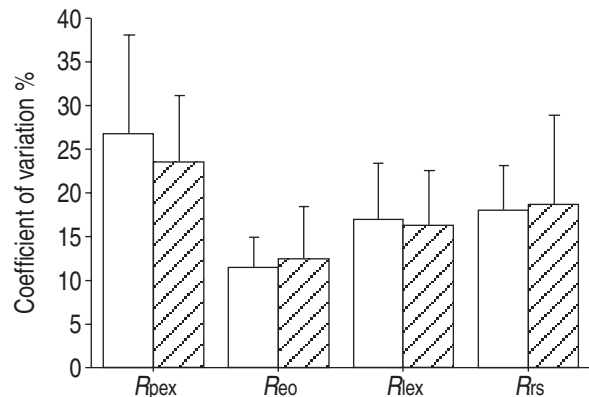
Fig. 3. – The coefficient of variation (CV) of interrupter resistance (R_{int}) data were significantly dependant upon the analysis technique used (Two way ANOVA: p<0.001). R_{pex} (R_{int} determined using polynomial back extrapolation method) and R_{lex} (R_{int} determined using linear back extrapolation method) were significantly more and less variable, respectively when compared to R_{eo} (instantaneous R_{int} following the end of pressure oscillations) and respiration system resistance (R_{rs}) (Pairwise comparisons: p<0.05). The mask type did not significantly influence the CV of R_{int} data. Columns (□: M_{comp}; ▨: M_{rigid}) and error bars represent mean and SD, respectively.

20 mL·s⁻¹ resulted in an interruption success rate of 100%. Group mean inspired volume in the breath immediately prior to occlusion was 30±1 mL (mean± SEM) and 32±1 mL, for M_{comp} and M_{rigid} respectively (paired t-test: p=0.052), with the volume during interruption being 90.7±1.6% and 92.5±0.4% of the inspired volume (paired t-test: p=0.27). The facemask used proved to have a major influence on R_{int}. Measurements using M_{comp} significantly underestimated R_{int}, independent of the analysis technique used (fig. 2). Analysis technique significantly influenced R_{int}, after accounting for the variation due to the

facemask (fig. 2). R_{pex} and R_{lex} were not significantly different from each other (R_{pex}: 3.86±0.2 kPa·L·s⁻¹, R_{lex}: 3.84±0.2 kPa·L·s⁻¹), however, both were significantly lower than R_{eo} (5.06±0.2 kPa·L·s⁻¹; p<0.05). R_{rs} was significantly higher than R_{int} values calculated from the remaining analysis techniques with a group mean of 16.88±1.25 kPa·L·s⁻¹ (p<0.05). Individual R_{int} data for M_{comp} and M_{rigid} are shown in table 1. The CV was significantly influenced by the choice of analysis technique (fig. 3). Group mean CV was lowest for R_{eo} (11.9±1.4%; p<0.05) and highest for R_{pex} (25.1±1.4%; p<0.05), while R_{rs} (18.4±1.4%)

Table 1. – Individual subject interrupter resistance data

Subject	R_{pex}		R_{lex}		R_{eo}		R_{rs}	
	M_{comp}	M_{rigid}	M_{comp}	M_{rigid}	M_{comp}	M_{rigid}	M_{comp}	M_{rigid}
1	1.87±0.95	6.91±0.81	2.16±0.59	6.81±0.89	3.63±0.54	7.51±1.02	17.25±3.15	13.81±2.64
2	2.58±0.94	4.11±0.75	2.78±0.55	3.85±0.21	4.02±0.56	4.68±0.35	16.16±.3.36	10.65±4.54
3	1.93±0.63	2.30±0.82	2.30±0.35	2.54±0.48	3.05±0.26	3.60±0.44	10.06±2.42	13.63±1.10
4	2.19±0.60	3.92±1.34	1.92±0.52	3.98±1.08	2.90±0.33	5.17±1.25	13.98±1.82	15.38±5.71
5	3.57±0.73	3.78±0.72	3.08±0.34	3.51±0.56	4.14±0.47	4.79±0.50	12.96±2.76	20.04±3.58
6	4.55±0.68	5.42±0.98	4.42±0.48	5.43±0.59	5.73±0.69	6.77±0.70	16.02±2.40	18.91±2.58
7	3.64±0.55	5.32±0.99	3.44±0.34	5.18±0.61	4.55±0.52	6.32±0.66	14.23±3.22	19.13±3.74
8	2.94±0.22	5.67±1.77	2.67±0.28	5.76±1.07	3.25±0.13	7.28±0.98	7.82±0.80	24.41±2.36
9	2.42±0.79	4.47±1.04	3.08±0.58	4.92±0.96	5.13±0.75	7.03±1.08	25.79±5.03	27.63±4.17
10	2.86±0.98	4.44±0.89	2.60±0.29	4.40±0.59	3.36±0.41	6.26±0.33	18.42±2.82	21.71±3.45
11	2.27±0.40	4.44±0.75	1.89±0.30	4.40±0.55	3.01±0.20	6.26±0.43	18.77±1.76	21.71±1.29
12	3.78±1.23	6.03±1.83	3.44±0.95	5.96±1.48	4.65±0.75	7.01±1.71	15.93±3.09	19.42±4.31
13	4.85±1.36	4.19±1.34	5.20±0.78	4.52±1.13	6.52±0.91	5.89±0.87	20.35±5.52	20.52±3.38
14	3.28±0.79	4.44±0.85	3.11±0.50	4.20±0.45	3.93±0.41	5.22±0.30	11.24±1.90	12.92±2.44
Mean±SEM	3.05±0.25	4.67±0.30	3.00±0.25	4.68±0.29	4.13±0.29	5.98±0.31	15.64±1.21	18.56±1.27

Individual interrupter resistance (R_{int}) (mean±SD) data for the four analysis techniques following the application of the large volume, compliant facemask (M_{comp}) and a small volume, rigid facemask (M_{rigid}). The analysis techniques were the: polynomial back extrapolation technique (R_{pex}), linear back extrapolation technique (R_{lex}), the mean instantaneous airway opening pressure (P_{ao}) after the pressure oscillations had ended (R_{eo}) and the mean P_{ao} at the end of the occlusion (R_{rs}).

and Rlex ($16.6\pm1.4\%$) were not different from each other.

Discussion

The primary purpose of this investigation was to evaluate the feasibility of using the interrupter technique in spontaneously breathing infants. This involved determining a suitable V'int, $t$int for infant studies and evaluating the influence of differing facemasks and analysis techniques on the magnitude and variability of Ppost and hence Rint. It could be demonstrated that the interrupter technique is feasible in healthy, unsedated infants. The choice of facemask plays a crucial role, with Mcomp causing a significant underestimation of Rint when compared to Mrigid. The method of determining Ppost also significantly influenced the variability and magnitude of Rint value.

Factors influencing suitable triggering

The most suitable V'int may be altered in infants, who have higher respiratory rates and lower tidal flows and volumes when compared to older children. The most appropriate trigger would be a stable volume landmark, thus ensuring a consistent lung volume during interruptions and minimizing the volume dependant effects of Rint. The disadvantage of a volume related trigger is the identification of a stable landmark, particularly in infants. The use of flow as a trigger reduces software and hardware delays as V' is directly measured while the V is calculated. The choice of 20 mL·s^{-1} for V'int produced occlusion volumes equating to $90.7\pm1.6\%$ and $92.5\pm0.4\%$ of the inspiratory volume for Mcomp and Mrigid, respectively. Indicating that reproducible lung volumes are feasible with a suitable V'int. PEF ranged between 33.1 and 73.3 mL·s^{-1} in this study group clearly indicating that V'int must be tailored to patient group to be tested. Thus the standardization of a specific triggering flow may not be possible, rather future studies should report the trigger flow, PEF and absolute and relative occlusion volumes to allow comparisons between study centres.

Influence of the facemask on interrupter resistance

Previous studies have demonstrated that the addition of a proximal compliance caused an underestimation of the Ppost [7, 8]. Simulating an unsupported airway, SLY et al. [7] reported an underestimation of Rint of up to 75.8%, which was reduced to a maximum error of 15.2% with a support airway. In older healthy and asthmatic children supporting the cheeks increased Rint by 20.5 and 32.7%, respectively [8]. These results suggest that as obstruction increases that the error introduced by a proximal compliance increases proportionally. The data in the present study confirm that increasing the proximal compliance (Mcomp) causes an underestimation of Rint in infants. The use of Mrigid increased Rint by values ranging from 18.7% (Rrs) to 55.7% (Rlex). These data illustrate the importance of minimizing the proximal compliance, indicating that the correct choice of facemask is an important factor in infant lung function studies. The use of a rigid walled mask will minimize the dead space and reduce compliance of the upper airways and measurement equipment.

Factors affecting the estimation of interrupter resistance

The main assumption of the interrupter technique is that Pao rapidly equilibrates with Palv during a brief airway closure. Lung inhomogeneities and Cua will influence the time for equalization of Pao and Palv. In older children and adults an interruption time of 80–100 ms is commonly used. The study of lung function in infants requires the use of a facemask placed over the nose and mouth. Thus the measured resistance of the airway tree will include the nasal pathway, which is known to contribute up to 49% of the measured airway resistance [18]. This additional resistance will significantly increase the time constant of the respiratory system and hence the occlusion time required to allow accurate confirmation of a relaxed passive system. In infants, the presence of the Hering-Breuer reflex allows longer occlusion times to be used and thus ensure that Palv equilibrates Pao, even in the presence of airway obstruction. The present study used an occlusion time of 500 ms, based on the occlusion time recommended for the single occlusion technique in infants [12]. Interruptions of this length were achievable in all infants without disturbing their sleeping patterns. The additional benefit of a longer occlusion time is that Rint calculated from Pao at the end of the interruption equates to Rrs, allowing estimates of both airway and respiratory resistances to be obtained. The method used to determine Ppost had an important effect on the magnitude and variability of Rint. Three of the analysis methods used allow the estimation of the resistance of the airway tree, namely Rpex, Rlex and Reo, while Rint calculated from the end of the interruption (Rrs) equates to the resistance of the airways and respiratory tissues, including the chest wall. Rpex and Rlex were not significantly different from each other and were both significantly lower than Reo. This is not unexpected as Reo is estimated from the instantaneous Pao at a fixed time point following the pressure oscillations, whereas Rpex and Rlex are determined from the back extrapolation of the Pao trace and thus derived from an earlier time point and hence lower Pao. Reo may overestimate Rint under conditions in which the concave shape of the Pao trace becomes more pronounced (i.e. airway obstruction), the value of Reo is also highly dependent on the time point chosen. The characteristics of the pressure oscillations are determined by the inertia and compressibility of the gas column [19, 20]. Alterations in the inertance and compliance of the airway wall will lead to changes in the frequency and damping of the pressure oscillations and may result in the time point chosen being invalid. The values of Rrs reported in the present

study are significantly higher than those reported in the literature. In a large cohort of infants (aged 2–10 weeks, group mean 5 weeks) studied prior to incidence of respiratory illness, YOUNG *et al.* [21] reported mean R_{rs} values of 5.6±0.1 kPa·L·s^{-1} (mean± SEM) using the single breath technique. Using the same technique, DUNDAS *et al.* [22] reported similar values of 5.3±1.7 kPa·L·s^{-1} (mean±SD) in healthy infants less than 13 weeks of age. The reasons for the differences between these previously reported values of R_{rs} and those in the present study (18.6±1.3; 10.7– 27.6 kPa·L·s^{-1} (mean±SEM; range)) using M$_{rigid}$ are not clear. The infants in the present study were unsedated, whereas previous investigations used sedation. Sedation is known to influence lung volumes and hence may influence lung mechanics. As far as the authors are aware there are no published data for the interrupter technique in young, unsedated infants and hence it is difficult to meaningfully compare the data with those R_{rs} data published with differing methodologies. However, in a group of healthy infants aged between 4.2 and 8 weeks RABBETTE *et al.* [23] reported end-inspiratory elastic recoil pressures ranging 0.78–1.02 kPa, which compares favourably to the end interruption P_{ao} determined with M$_{rigid}$ in the present study (0.59–1.06 kPa).

In agreement with previous studies in children and adults R_{pex} was significantly more variable than the remaining estimation techniques [2, 10]. Furthermore, as reported by PHAGOO *et al.* [2] in five-year-old children, R_{lex} was the least variable. As the subjects in the present study were healthy, unsedated infants it was not possible to carry out challenge testing for ethical reasons, and as such no direct conclusions as to the most sensitive and appropriate interrupter analysis method for challenge testing can be made.

In summary aspects of measurement set-up and subsequent analysis influence the accuracy, technical feasibility and variability of the interrupter technique when applied to an infant population were examined. The study demonstrated that the interrupter technique is feasible in spontaneously breathing, sleeping infants. The ability to apply the interrupter technique to an unsedated, sleeping infant population could potentially allow the technique to be used for large epidemiological studies. Also of importance may be the application of the technique for the clinical monitoring of infants with asthma and other respiratory diseases. Occlusions of 500 ms could be applied with no respiratory muscle activity present in the majority of interruptions. The choice of facemask in this age group significantly influenced the subsequent R_{int} values and future studies should use rigid wall, non-compliant masks. The reduction of dead space through the use of suitable putty would also be desirable. It was demonstrated that the linear extrapolation method was the least variable analysis technique. Future use of the interrupter technique will need to report factors that are known to influence the outcome of R_{int} studies, including facemask type and dead space, the analysis technique, occlusion length and the flow at which the occlusion is triggered. Ideally these factors should be standardized, at least within specified age ranges, allowing reference data to

be generated that may be used by a number of study centres. Challenge testing in infants of this age remains to be carried out to confirm the clinical usefulness of the interrupter technique in spontaneously breathing infants.

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