RESPIRATORY PHYSIOLOGY

Short and long term variability of the interrupter technique under field and standardised conditions in 3–6 year old children

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Background: The short and long term variability of the interrupter technique was assessed to determine whether interrupter resistance is a stable individual characteristic over time. The effect of field and standardised measurement conditions on the within-subject variability of the interrupter technique was also examined.

Methods: The interrupter technique was studied under field and standardised conditions in children aged 3–6 years. Under field conditions, five investigators performed the measurements using two different measurement devices in random sequence. Both short term (20–30 minutes) and long term variability (median 38 days) were assessed in 32 children. Under standardised conditions, a single investigator conducted all measurements using a single device; the repeated measurements were conducted at the same time of day in a familiar quiet classroom. Long term variability (median 11 days) was estimated in 15 children. Within-subject standard deviations were estimated by analysis of variance with adjustment for the effects of different investigators and measurement devices on within-subject variability under field conditions.

Results: Under field conditions within-subject standard deviations for short and long term variability were 0.10 kPa/l/s (adjusted 0.10 kPa/l/s) and 0.13 kPa/l/s (adjusted 0.14 kPa/l/s), respectively. Under standardised conditions the within-subject standard deviation for long term variability was 0.10 kPa/l/s.

Conclusions: Measurement of interrupter resistance under field conditions only slightly increased the within-subject variability compared with standardised conditions. The results indicate that interrupter resistance is a stable individual characteristic over a period of some weeks.

The interrupter technique is a potentially useful clinical and research tool for objective measurements of airway resistance in very young children. The technique is performed during normal quiet breathing, requires minimal cooperation, and is non-invasive.[1–4]

The suitability of the interrupter technique in young children has been investigated in several studies,[3 5–10] but most of these primarily included wheezy or asthmatic children or studied the overall variability of the interrupter technique. The overall variability, however, depends on within-subject variability as well as between-subject variability, the latter being determined by the heterogeneity of the study population—for example, in age or height. Moreover, only one study has so far assessed variability of the interrupter technique over some weeks.[11] The first aim of this study was to assess within-subject variability of the interrupter technique over a period of 20–30 minutes and over a period of some weeks by estimating within-subject standard deviations by analysis of variance, to evaluate whether interrupter resistance is a stable individual characteristic over time. A small within-subject variability is important in evaluating the effect of a therapeutic intervention. Furthermore, in most studies which assessed the variability of the interrupter technique, a single investigator performed all measurements and used a single measurement device. A second aim of this study was therefore to investigate the extent to which the within-subject variability was affected by measurement of interrupter resistance under field conditions, as opposed to standardised conditions where all measurements were conducted by a single investigator using a single device and where the repeated measurements were conducted at the same time of day in a familiar and quiet classroom. The interrupter technique is only suitable in epidemiological studies when variability over time under field conditions is acceptable.

METHODS

Two studies were conducted to evaluate the interrupter technique under field conditions (study A) and under standardised conditions (study B). In study A both short term (within-subject variability over a period of 20–30 minutes) and long term variability (within-subject variability over a period of some weeks) were examined, and in study B only long term variability was assessed. Variability is defined as the degree of agreement between repeated individual interrupter resistance measurements—that is, whether interrupter resistance is a stable individual characteristic between two measurements and whether the repeatability of repeated measurements is good.

The studies were approved by the medical ethics committees involved (as part of larger studies) and written consent was given by the parents of the participating children.

Subjects

Study A: Variability under field conditions

Thirty two children were randomly selected from an ongoing cohort study. None had signs of eczema or had respiratory symptoms at the time of interrupter resistance measurement; this study population can therefore be regarded as a general population sample.[12] None of the children had a history of asthma, but in 12 cases the parents reported wheeze in early life.

Table 1 Baseline characteristics of the children in the study performed under field conditions (study A) and in the study performed under standardised conditions (study B)

	Population measured under field conditions		Population measured under standardised conditions
	Short term variability (n=32)	Long term variability (n=25)	Long term variability (n=15)
No of boys	17	12	8
Age (years)	4.3 (0.2) (3.7–4.9)	4.3 (0.3) (3.7–4.9)	4.6 (1.0) (3.2–5.9)
Height (cm)	106.3 (4.5) (98.0–119.0)	105.7 (3.6) (98.0–111.0)	110.9 (7.0) (97.5–122.9)
Weight (kg)	18.8 (2.5) (14.9–24.7)	18.5 (2.5) (14.9–24.7)	19.0 (2.7) (15.0–23.7)

Values are mean (SD), range.

Study B: Variability under standardised conditions

The study population measured under standardised conditions consisted of 15 healthy children randomly selected from a daycare centre and a kindergarten. These children had no history of any cardiorespiratory disease and had no respiratory symptoms at the time of the study.

Measurement of interrupter resistance

Expiratory interrupter resistance was measured by the interrupter technique using a commercial device (MicroRint, Micromedical Ltd, UK) because expiratory interrupter resistance seems slightly more sensitive in detecting (subclinical) differences in airway calibre within and between subjects than inspiratory interrupter resistance.[1] The children were carefully instructed how to perform the test. During the test the children were sitting and were quietly breathing through the device via a mouthpiece with a nose clip, the lips firmly sealed around the mouthpiece, and the neck slightly extended. The cheeks and throat were supported by the hands of the investigator standing behind the child in order to decrease upper airway compliance.[13] Optimal passive cooperation by the children was enhanced by showing a video movie. After a period of quiet breathing, a single expiratory interruption was triggered at the peak of tidal flow during 100 ms.[5 6] The children were unable to anticipate the trigger event but were able to hear the valve closing.

In each subject 10 occlusions were performed and the median of five or more technically satisfactory readings was taken as a valid measurement. If necessary, the procedure was repeated until at least five acceptable readings were obtained. Attempts were not accepted if the mouth pressure-time curve and/or flow-time curve did not fulfil criteria as described in the literature,[9 14] or if the child did not breathe quietly. The median resistance value, number of completed interruptions, reasons for failure, and a subjective judgement of the measurement quality by the investigator were recorded. This protocol was used in both study groups.

Variability was assessed in children with no respiratory symptoms and no use of respiratory drugs during the 12 hours before the test on both measurement days. There was no difference in respiratory symptoms on the different measurement days in the children in either study group.

Study A: Variability under field conditions

Interrupter resistance was measured at the homes of the 32 children. Two measurements, 20–30 minutes apart, were performed to assess short term variability. To evaluate long term variability a third measurement was conducted a few weeks after the first measurement (median 38 days, range 22–77). It was possible to conduct a third measurement in 25 of the 32 children. Because the interrupter technique was studied under field conditions, five different investigators performed the measurements using two different measurement devices (both MicroRint) in random sequence. A short questionnaire was administered on the child's health status during the previous 2 weeks and on medication use 12 hours before the measurement.

Study B: Variability under standardised conditions

Measurement of interrupter resistance in study B was conducted according to the same protocol as in study A. However, in this study the interrupter resistance was measured under standardised conditions—that is, all measurements were conducted by a single investigator using a single device for all measurements. Repeated measurements were also conducted at the same time of the day and were carried out in a familiar and quiet classroom. Two measurements were made in 15 healthy children to evaluate long term variability. The median interval between the two measurements was 11 days (range 7–13).

Data analysis

Analysis of variance was conducted to estimate within-subject standard deviations (SD_w) for short and long term variability of the interrupter technique. SD_w is the usual measure of variability when within-day or between-day variability is studied.[15] It was calculated from the analysis of variance results as the square root of the pooled within-subject sum of squares divided by its degrees of freedom.[15] In the study under field conditions, adjustment was made for the effects of different investigators and measurement devices on within-subject variability by including these factors as independent variables in the model.

The underlying assumption of the model is that variability is independent of the level of interrupter resistance. To examine this assumption, the differences between paired measurements were plotted against their means (Bland-Altman plot).[16]

RESULTS

The characteristics of the two study populations are shown in table 1. The children and their parents readily accepted the tests.

Bland-Altman plots of individual differences between paired measurements against their mean interrupter resistance values are shown in fig 1 for measurements under field conditions using a short term interval (fig 1A) and a long term interval (fig 1B) between paired measurements. Variability was found to be independent of the level of interrupter resistance in both study populations ($p>0.8$ for regressions of differences against means).

Mean baseline values of interrupter resistance, mean baseline interrupter resistance Z scores, and SD_w values are shown in table 2. Under field conditions the SD_w for long term variability was slightly higher than for short term variability. The SD_w for long term variability under field conditions was also only slightly higher than the SD_w for long term variability under standardised conditions.

Adjusting for the effects of different investigators and different measurement devices hardly changed the within-subject variability results in the study under field conditions.

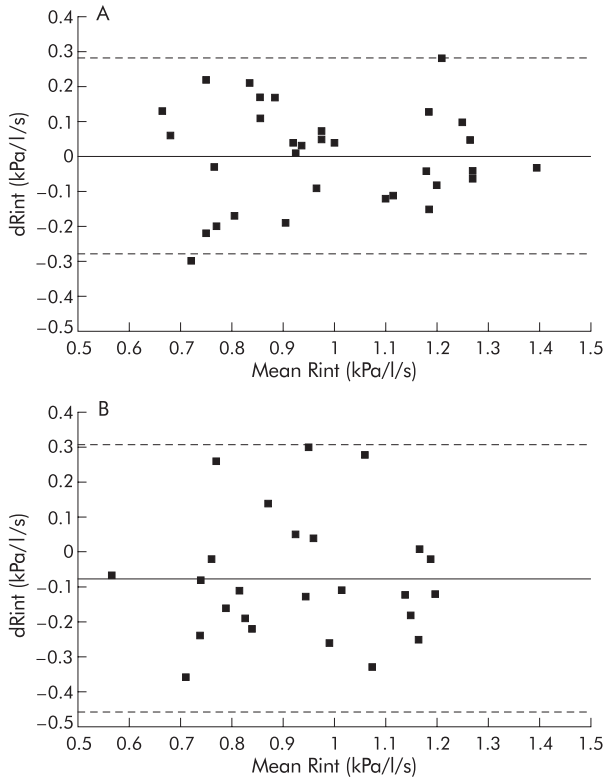

Figure 1 Bland-Altman plots of individual differences between paired measurements against mean values of interrupter resistance (Rint) under field conditions using (A) a short term interval (20–30 minutes) and (B) a long term interval (several weeks) between paired measurements. The solid lines indicate the mean difference between paired measurements and the dashed lines indicate 95% limits of agreement.

Adjusted SD_w values for short and long term variability in the study under field conditions were 0.10 kPa/l/s and 0.14 kPa/l/s, respectively, with no significant effects of different investigators and measurement devices in the models.

DISCUSSION

Our study has shown that within-subject variability of the interrupter technique over a period of some weeks was comparable to within-subject variability over a period of 20–30 minutes, indicating that interrupter resistance may be a stable individual characteristic over a period of some weeks. The repeatability of interrupter resistance measurements over both short and long term intervals was satisfactory. Furthermore, within-subject variability over a period of some weeks under field conditions was only slightly higher than under standardised conditions, in spite of the fact that five observers and two pieces of equipment were involved.

The SD_w for short term variability was found to be comparable to the SD_w reported by others. Previous studies considered short term variability satisfactory, where a low SD_w indicates a small variability over time. Klug *et al*[6] found an SD_w for short term variability of 0.08 kPa/l/s in healthy children 2–7 years of age. Furthermore, an SD_w of 0.14 kPa/l/s was reported for short term variability in asthmatic children.[8]

A recent study by Lombardi *et al*[11] studied the long term repeatability of the interrupter technique in 26 children with a history of either cough or wheeze, with a mean interval of 2.5 months between the two measurements. Interrupter resistance repeatability was defined as two standard deviations of the paired differences between the two sets of measurements and was estimated as 0.21 kPa/l/s. The results of our study show that, although assessed in healthy children and with different statistical analysis methods, long term variability was comparable with that estimated by Lombardi *et al*. This may suggest that interrupter resistance is a stable individual characteristic, even over a longer period of time. This is important, for instance, in studying long term effects of an intervention on interrupter resistance.

For studying the effects of an intervention and a placebo on interrupter resistance in a clinical trial, the required number of subjects in both groups can be calculated.[17] With a common variance of 0.04 kPa/l/s in the two groups (calculated from the observed standard deviation of 0.2 kPa/l/s (table 2)), a significance level of 0.05, and a power of 80%, 28 subjects are required in each group to detect a difference of 0.15 kPa/l/s between the effects in both groups.

Because we investigated variability of the interrupter technique in study A under field conditions, several factors such as different investigators, different measurement devices, and measurement at different times of the day may have randomly influenced within-subject long term variability.[1 6 13 18] In study B the conditions during which interrupter resistance was measured were standardised—that is, a single investigator conducted the measurements using a single device and the investigator and device were stable during the measurements. Furthermore, the repeated measurements were conducted at the same time of day in a familiar and quiet classroom. The within-subject variability results hardly changed after adjustment for the effects of different investigators and different measurement devices on within-subject variability in study A, and both unadjusted and adjusted long term within-subject variability in the study under field conditions was only slightly higher than under standardised conditions. This indicates that the measurement conditions had little influence on variability.

The clinical characteristics of the children might have differed between the two study groups. None of the children measured under standardised conditions in study B had a history of any cardiorespiratory disease or current respiratory symptoms. The 32 children in study A had no history of asthma, signs of eczema, or respiratory symptoms at the time the measurements were made, but 12 of them had a history of wheezing or whistling in the chest. The mean baseline

Table 2 Within-subject variability of the interrupter technique

	Population measured under field conditions		Population measured under standardised conditions
	Short term variability	Long term variability	Long term variability
Mean (SD), range baseline Rint (kPa/l/s)	0.99 (0.22) (0.60–1.41)	0.97 (0.20) (0.60–1.29)	0.85 (0.21) (0.55–1.31)
Mean baseline Rint Z score*	0.59	0.41	0.11
SD_w (kPa/l/s)	0.10	0.13	0.10

Rint=interrupter resistance; SD_w=within-subject standard deviation.
*Z scores calculated as (measured Rint – predicted Rint)/(RSD of the reference population). Predicted Rint values calculated based on regression equation by Merkus *et al*.[1]

interrupter resistance Z scores were higher in the study performed under field conditions than in the study performed under standardised conditions. However, in all the children in both study groups there was no difference in respiratory symptoms between different measurement days.

Another difference between the two study groups was that different time intervals between the two measurements were used to evaluate variability (median 38 days in study A and 11 days in study B). A longer time interval between two measurements might increase variability.[15]

In conclusion, our study suggests that interrupter resistance is a stable individual characteristic over time, given the satisfactory within-subject standard deviations for both variability over a period of 20–30 minutes and over a period of some weeks. Measurement under field conditions only slightly increased the within-subject variability compared with standardised conditions, indicating that the interrupter technique is suitable for use in clinical and epidemiological studies where observer, measurement device, and time of measurement cannot always be controlled.

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