CHAPTER 3

Correction factors for oxygen and flow-rate effects on neonatal Fleisch and Lilly pneumotachometers

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3.1. Abstract

Objective: To assess the effects of different oxygen concentrations and flow rates on the measurement errors of neonatal pneumotachometers in heated and unheated situations, and to develop correction factors to correct for these effects.

Design: Prospective laboratory study.

Setting: Outpatient clinic with equipment in a standardized setting.

Subjects: Neonatal pneumotachometers.

Interventions: In standardized conditions the tested pneumotachometer was calibrated at a flow rate of 3 L/min with 60 per cent oxygen and was set in series with a closed spirometer system being used as a reference. Different airflow levels (1–9 L/min) and oxygen concentrations (21–100%) were infused into the closed system with pneumotachometer and spirometer.

Measurements and Main Results: The pneumotachometers were significantly affected by changing oxygen concentrations \((p<0.01)\) and increasing flow rates \((p<0.01)\) increasing the actually measured flow rate. Correction factors, developed by multiple regression analysis, significantly reduced the overall maximum errors of the pneumotachometers from -1.1–0.6 L/min to -0.5–0.4 L/min.

Conclusions: The effects of changes in oxygen concentrations and flow rates on neonatal pneumotachometers could be considerably decreased by the use of correction factors as were calculated in this study. This will preclude frequent calibration procedures with actual flow and oxygen levels during changes in experimental settings.

3.2. Introduction

In research as well as in clinical practice, accurate measurements of respiratory gas flow rates are important. Pneumotachometers are used in set-ups for estimating lung volumes, respiratory system compliance and resistance. Pneumotachometers can be based on several principles, like linear resistive pneumotachometers, turbine flowmeters, thermal devices, ultrasonic flowmeters, polyvinylidene fluoride piezoelectric film flowmeters, non-linear differential pressure-based transducers, linear differential pressure devices and flow plethysmography. Since the dead space of pneumotachometers has been sufficiently reduced they can be used in neonates. There are, however, more specific conditions to be taken into account during lung function testing in neonates, especially when they are mechanically ventilated. According to Hagen-Poiseuille’s law, changes in physical characteristics of a respiratory gas (composition, temperature, relative humidity, and pressure) directly affect pneumotachometer flow measurements.
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$$pD = \frac{(8 \cdot L \cdot \eta \cdot v)}{(\pi \cdot r^4)}$$

Where $pD$ is the decrease in pressure; $L$ the length of tube over which pressure decrease is measured; $\eta$ the viscosity of gas; $v$ the velocity; and $r$ the radius of tube over which pressure decrease is measured.

In addition, turbulence, the geometry of the tubes connecting the pneumotachometers and the dimensions of the resistive element influence flow recordings by pneumotachometers. In experimental settings at a neonatal intensive care unit (NICU) water can accumulate on the resistive element of pneumotachometers increasing resistance and causing turbulence, leading to measurement errors. Heating of the pneumotachometer diminishes this effect. In the NICU flow rates and oxygen concentrations are often changed leading to a varied accuracy of flow signals. In recently developed neonatal ventilators algorithms are incorporated to reduce the measurement error of their pneumotachometers. However, most of them (Stephanie and Dräger among other companies) only include corrections for body temperature and pressure saturated with H2O vapour (BTPS). The Viasys Avea and the VIP Bird neonatal and paediatric ventilators additionally correct for altitude (barometric pressure). However, to our best knowledge, no correction is made for actual oxygen concentration and flow rate. We investigated the accuracy of the two most frequently used neonatal pneumotachometers to measure lung function in experimental settings. Both are based on the linear resistive principle: a Fleisch type pneumotachometer (consisting of parallel capillary tubes) and a Lilly type pneumotachometer (containing a fine wire mesh screen). We studied measurement errors secondary to changing measurement conditions (e.g. flow rate, oxygen concentration and heating of the devices). Correction factors were calculated in order to prevent the need for frequent calibration procedures at actual flow rates and oxygen concentrations.

3.3. Material and methods

A Lilly pneumotachometer (8410A, Hans Rudolph Inc., Kansas City, MO; linear range 0–10 L/min) and a Fleisch pneumotachometer (No. 00, General Medical Corp., Erie, PA; linear range 0–9 L/min) were tested. Pressure differences across the resistive element of both pneumotachometers were measured with a differential pressure transducer (type 163PC01D75, Honeywell, Morristown, NJ). Air and oxygen from the hospital circuit were mixed with an oxygen-air mixer (961 Siemens-Elema, Siemens, The Hague, The Netherlands) and flow rates were roughly set by a rotameter (Air 0–15 L/min, Medec, Aalst, Belgium) (Figure 1).
The oxygen concentration (at 30 cm before the pneumotachometer) as well as the temperature (at 80 cm after the pneumotachometer) inside the system were recorded by an oxygen meter (Teledyne TED 60T, Teledyne Brown Engineering, Huntsville, Alabama) and a thermometer (Fluke 51 K/J thermometer, Fluke Nederland B.V., Eindhoven, The Netherlands), respectively. A 10-litre-rolling-seal spirometer (Masterscreen-FRC Jaeger complete system, Erich Jaeger GmbH, Hoechberg, Germany) was used as a gold standard for volume against time. Connections between different parts of the equipment were formed by ribbed rubber tubes with an inner diameter of 2 cm and an outer diameter of 2.9 cm before and after the pneumotachometer, and the standard ribbed tubes belonging to the spirometer with an inner diameter of 3.0 cm and an outer diameter of 3.2 cm connected the former tubes from the point of temperature assessment to the spirometer. Flow signals from the pneumotachometers were processed by computer using the software package RASP (Respiratory Analysis System Program, Physio Logic, High Clere, Great Britain).

We calibrated the pneumotachometer system at an oxygen concentration of 60 per cent to keep the maximum error, expected to be caused by the most extreme oxygen concentrations, as small as possible. Flow calibration was performed at zero flow and at a maximum of 3 L/min according to the spirometer. Since flow rates measured by the spirometer can only be determined afterwards all measured values were multiplied with a new calibration factor determined afterwards at 3 L/min and 60 per cent oxygen. This calibration procedure was performed for each measurement session separately.

At the start of the measurements an oxygen concentration of 21 per cent and a steady flow rate of about 1 L/min (according to the spirometer) was used. We repeated the same procedure at an oxygen concentration of 21 per cent and a steady flow rate of 2 L/min, followed by 3, 4, 6 and 9 L/min. Afterwards we tested the other oxygen concentrations of 30, 40, 50, 60, 70, 80, 90 and 100 per cent at the same steady
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flow rates. We repeated half the session, i.e. the same measurement procedures in the opposite order at 100, 80, 60, 40 and 21 per cent oxygen every time at 1, 3, 6 and 9 L/min.

The complete procedure was performed for each pneumotachometer, i.e. the Lilly and the Fleisch pneumotachometer heated as well as unheated. Recordings during every measurement were continued until the spirometer with a volume of 10 L was completely filled, except at a flow rate of 1 L/min a maximum total volume of 6 L mean was achieved. No lower volumes were accepted to prevent measurement errors due to a potential inaccuracy of the spirometer. Before and after each measurement procedure calibration settings were checked with a precision syringe of 50 ml independently from the spirometer.

When this check revealed an error of more than 2.5 per cent the whole measurement procedure was repeated. Paired-samples \( t \)-tests were performed to estimate significant differences of the measurement errors between calibration level and the lowest and highest oxygen concentrations and flow rates. Bonferroni correction for multiple comparisons was performed.

Multiple regression analyses were used to derive correction equations for each pneumotachometer. We used a stepwise forward regression technique with the reference flow (i.e. the flow recorded by the spirometer) as the dependent variable. The flow measured by the pneumotachometer, its product term with the oxygen concentration and its square were included as independent variables. Variables were added on the basis of statistical significance (\( p<0.05 \)) or when they substantially improved the fit of the model, according to the distribution of the residuals left. To enable comparison between pneumotachometers data were presented as relative measurement errors calculated from the regression equations. This means that the differences between the flow rates measured by the pneumotachometer and the calculated spirometer flow rates (dependent variable in regression equation) after entering the pneumotachometer flows in the equations were presented. These differences were divided by the spirometer values and expressed as percentages. Since variances explained by the regression equations were very high (\( R^2>0.99 \)) no important deviation from the real measured data was to be expected. To test the improvement due to the use of the correction factors following from the regression equations Bland&Altman plots \(^{20} \) were used in which the differences between spirometer and pneumotachometer were plotted against the mean of their flow rates. The paired samples \( t \)-test was again used to estimate any significant improvements due to the use of these correction factors.

Polynomials of different pneumotachometer flow errors relative to spirometer flow were calculated with the multiple regression equations using arbitrary oxygen concentrations and flow rates. The Statistical Product and Service Solutions 10.0 (SPSS Inc, Chicago, IL, USA) for Windows was used for the statistical calculations.
3.4. Results

The temperature measured inside the closed circuit at 80 cm after the pneumotachometer did not change by more than 1.3°C (ranges for each experiment, 21.9–23.2; 20.2–21.1; 21.1–21.7; 20.3–21.4) for the unheated pneumotachometers and not more than 2.4°C (ranges for each experiment, 20.7–23.1; 20.6–21.7; 22.1–23.1; 21.3–23.1) for the heated pneumotachometers within each experiment. Changes of barometric pressure and humidity during the measurement procedures were not present or very small reaching maximum values of 0.2 kPa and 4 per cent, respectively.

Figure 2. Trends of relative measurement errors of the pneumotachometers (PNT) at the calibrated flow rate (3 L/min) at different oxygen concentrations.

Figure 3. Trends of relative measurement errors of the pneumotachometers (PNT) at the calibrated oxygen concentration (60%) at different flow rates.
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Considerable effects of oxygen concentration, shown in Figure 2, were underlined by the relative error being significantly different at 21 and 100 per cent oxygen (at 3 L/min) compared to calibration level (60 per cent oxygen at 3 L/min) in all pneumotachometers ($p<0.02$). All pneumotachometers showed a comparable increase of the relative measurement error at rising oxygen concentrations, the most prominent for the unheated Lilly pneumotachometer. However, differences between pneumotachometers were small. Compared to calibration level (3 L/min at 60 per cent oxygen) the measurement errors were significantly different at 1 L/min and 9 L/min at 60 per cent oxygen in all pneumotachometers ($p<0.02$) (Figure 3). An increasing measurement error became apparent in all pneumotachometers above calibration flow rate. The relative measurement error also increased at lower flow rates. Again differences between pneumotachometers were relatively small.

Multiple regression analyses yielded correction equations for each pneumotachometer (Table 1). With these regression equations a corrected flow could be calculated from the measured flow at different levels of oxygen concentration and

<table>
<thead>
<tr>
<th>Pneumotachometer</th>
<th>Regression Equation</th>
<th>$r^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heated Fleisch</td>
<td>Flow$_R$ = 1.10·Flow$_M$ - 0.0013·Flow$_M$·O$_2$% - 0.086·(Flow$_M$)$^2$</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Unheated Fleisch</td>
<td>Flow$_R$ = 1.10·Flow$_M$ - 0.0013·Flow$_M$·O$_2$% - 0.015·(Flow$_M$)$^2$</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Heated Lilly</td>
<td>Flow$_R$ = 1.11·Flow$_M$ - 0.0013·Flow$_M$·O$_2$% - 0.011·(Flow$_M$)$^2$</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Unheated Lilly</td>
<td>Flow$_R$ = 1.14·Flow$_M$ - 0.0013·Flow$_M$·O$_2$% - 0.014·(Flow$_M$)$^2$</td>
<td>&gt;.99</td>
</tr>
</tbody>
</table>

$^a$Flow$_{REAL}$ = spirometer flow (L/min); $^b$Flow$_{MEASURED}$ = pneumotachometer flow (L/min).

<table>
<thead>
<tr>
<th>Pneumotachometer</th>
<th>Mean difference</th>
<th>Limits of Agreement</th>
<th>Maximum Error Range (difference)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before correction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heated Fleisch</td>
<td>-0.18</td>
<td>-0.83, 0.46</td>
<td>-1.09, 0.40 (1.5)</td>
</tr>
<tr>
<td>Unheated Fleisch</td>
<td>-0.20</td>
<td>-1.02, 0.62</td>
<td>-1.26, 0.51 (1.8)</td>
</tr>
<tr>
<td>Heated Lilly</td>
<td>-0.36</td>
<td>-1.33, 0.61</td>
<td>-1.08, 0.17 (1.3)</td>
</tr>
<tr>
<td>Unheated Lilly</td>
<td>-0.13</td>
<td>-1.01, 0.74</td>
<td>-1.28, 0.58 (1.9)</td>
</tr>
</tbody>
</table>

| After correction  |                |                     |                                  |
| Heated Fleisch    | -0.01          | -0.26, 0.24         | -0.28, 0.35 (0.6)               |
| Unheated Fleish   | -0.01          | -0.34, 0.31         | -0.29, 0.39 (0.7)               |
| Heated Lilly      | -0.04          | -0.32, 0.24         | -0.51, 0.37 (0.9)               |
| Unheated Lilly    | -0.02          | -0.28, 0.24         | -0.46, 0.37 (0.8)               |
flow rate. As illustrated in Table 2, correction of the measured values with pneumotachometers resulted in a significant decrease of the measurement errors ($p<0.03$) in all pneumotachometers. Before correction a mean measurement error varied between -0.13 and -0.36 L/min depending on the pneumotachometer tested. After correction this was significantly reduced to -0.01 and -0.04 L/min. Limits of agreement, corresponding with two standard deviations of the differences between pneumotachometer and spirometer, even exceeded 1 L/min in some cases, while these limits remained below 0.40 L/min after correction. Maximal error ranges showed a comparable pattern. To avoid the use of these complex correction equations in practice we calculated polynomials to estimate the relative measurement errors at arbitrary oxygen concentrations and flow rates (Figure 4).

The heated Fleisch pneumotachometer showed the most dispersed polynomials in horizontal direction indicating that the relative measurement error did not increase as fast at rising flow levels as it did in the heated and unheated Lilly pneumotachometers and the unheated Fleisch pneumotachometer. The heated Fleisch curve in Figure 3 also seemed to be the flattest. Judging the dispersion of the curves in Figure 4 in vertical direction the increase of the measurement errors based upon a rise

![Figure 4](image_url)

*Figure 4.* Relative measurement errors of the pneumotachometers relative to the reference flow rate of the spirometer plotted as polynomials according to oxygen concentration and flow rate. Underestimation of flow rates by the pneumotachometer is indicated as a negative relative error and overestimation of flow rates as a positive relative error.
in oxygen concentration was most obvious in the unheated Lilly pneumotachometer and least obvious in the unheated Fleisch pneumotachometer. This was also demonstrated in Figure 2.

3.5. Discussion

Both the Fleisch and Lilly pneumotachometers were significantly affected by increasing oxygen concentrations from 21 to 100 per cent and increasing flow rates from 1 to 9 L/min increasing the actually measured flow rate in the heated as well as in the unheated situation. Multiple regression analysis yielded correction factors to correct for these effects resulting in a significantly improved accuracy of the flow measurements in almost all pneumotachometers. This means that after a calibration at 0 and 3 L/min and 60 per cent oxygen and correction for the influences of oxygen and flow rate reliable flow measurements can be achieved in the appropriate flow range and at all oxygen concentrations with these neonatal pneumotachometers.

Although linear resistance pneumotachometers are supposed to be used heated to avoid water accumulation, we tested them unheated as well. In practice sometimes unheated probes are used. Therefore, it would be interesting to correct for measurement errors caused by differences in heating assuming that no detectable water accumulation had occurred in the unheated situation. Our results confirmed that when heated pneumotachometers were used the error caused by flow rates, but not by oxygen concentrations, was less compared to when they were tested unheated. However, the actual gas temperature measured behind the heated pneumotachometer was also flow dependent. At lower flow rates the gas had more time to warm up compared to higher flow rates. Hence, the temperature difference that we measured between low (1 L/min) and high (9 L/min) flow rates was 10°C for the heated Fleisch pneumotachometer (40.0 to 29.9°C). For the heated Lilly pneumotachometer the maximum temperature difference was 5°C (30–24.9°C). Maximal temperature differences of 10°C and 5°C cause maximal viscosity changes of 2.6 per cent and 1.3 per cent, respectively. Temperature decreased at higher flow rates. So, levelling temperatures at all flows implies that the temperature at high flow rates should increase or the temperature at low flows should decrease. Increasing the temperature at high flows will increase gas viscosity and, thereby, the measurement error. The other possibility, decreasing temperature at low flow rates, results in the negative flow error to be increased. In both cases the slope of the lines of both heated pneumotachometers will rise approximating the ones of the unheated pneumotachometers.

Environmental changes during our experiments, like changes in temperature, barometric pressure and humidity outside the closed circuit, were negligible because changes were minimal and because calibration procedures were performed before
each measurement procedure. The maximum changes in humidity would have caused a decrease in viscosity of 0.1 per cent. Barometric pressure changes would only give a measurable effect on viscosity when exceeding 500 kPa,\textsuperscript{69} which it did not during our measurements. Because before each single measurement calibration was performed the effect caused by a slightly different connection of the tubes to the pneumotachometers could be ignored. Furthermore, changes in temperature inside the spirometer during heating of the pneumotachometers could be neglected. After being heated by the pneumotachometer to temperatures above 25°C, air cools down to room temperature by the time it reached the spirometer, which was 160 cm further in the circuit. The maximum temperature 23.2°C measured at 80 cm behind the pneumotachometer, where the thermometer was located, proved that the air equilibrated quickly to room temperature (22°C). When, for example at a NICU, the oxygen concentration in inspiratory air is increased, the viscosity of this gas mixture increases and thereby causes the pneumotachometers to overestimate flow rates.\textsuperscript{97} This effect was confirmed by our results presenting a progressive measurement error at increasing oxygen concentrations. Because differences between pneumotachometers were relatively small and because they were not considered as the purpose of this study, a thorough discussion concerning the potential causes did not seem appropriate.

In equipment based on differential pressure, like pneumotachometers, turbulence can cause a considerable error, thereby overestimating flow rates. Frey et al.\textsuperscript{73} indicated that the physical properties of most pneumotachometers usually cause a non-linear relationship between the applied and measured signals. According to Yeh et al.\textsuperscript{269} flow-conductance characteristics of differential pressure pneumotachometers are non-linear. Finucane et al.\textsuperscript{67} observed a non-linearity in screen pneumotachometers as well as in Fleisch type pneumotachometers. Our data showed that flow errors in all pneumotachometers increased considerably when flow rates were progressively higher than calibration flow rate. Pneumotachometers underestimated at flow rates lower than calibration flow of 3 L/min.

Although constant in the absolute way, this small error increased relatively at lower flow rates. Noise in the recorded signals probably caused the most important part of this measurement error. Although the used pneumotachometers should be linear within the flow range measured, non-linearity of the pneumotachometers within this range was, to our opinion, the most plausible explanation for the error pattern that was found. Differences between pneumotachometers were again relatively small and were therefore not considered for discussion.

The correction factors, following the multiple regression equations for each heated and unheated pneumotachometer separately, reduced the measurement errors significantly in all pneumotachometers. Maximal error ranges were reduced by more than 50 per cent in most pneumotachometers. Peak flow rates in preterm neonates might exceed 6 L/min in some cases. If we assume that flow rates in preterm infants
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varied between 0 and 6 L/min, according to our results, a measurement error of ±9 per cent could be expected when no correction was performed (±5 per cent because of the oxygen effect plus ±4 per cent caused by the flow rate effect). After correction for oxygen and flow effects a residual effect of ±2 per cent caused by variance in oxygen concentration and flow rate could be expected within a flow range of 0–6 L/min. The pneumotachometers we tested are predominantly used in research settings to measure lung function (compliance, resistance, forced expiratory flow rates, etc.) in preterm infants. The role of lung function testing in improving ventilator adjustments, and diagnosis and prognosis of respiratory morbidity in neonates has been investigated increasingly during recent years. Consequently, lung function measures like respiratory resistance, which is highly flow dependent, will become more accurate after correction. Some mechanical ventilators use comparable pneumotachometers. When the same pneumotachometers are used as described above the built-in corrections for BTPS might be extended with corrections for oxygen concentrations and flow rates based on our results. Integral application of the regression equations will be necessary for a reliable correction during conditions of changing flow.

Correction factors were based upon measurements with dry gases at 22°C, which were sufficiently constant during our measurement procedures. Because of their opposite effects on the viscosity of a gas a simultaneous increase of humidity and temperature from dry air in the hospital circuit during calibration procedures (relative humidity approximating 0 per cent at 22°C) to a humidified and warmed environment (relative humidity 95 per cent at 37°C) will result in a measurement error of approximately 2.9 per cent (4.1 per cent caused by the increase of temperature and -1.2 per cent caused by the increased humidity). This implicates that besides corrections for the effects of oxygen concentrations and flow rates humidity and temperature effects should be corrected for when flow measurements are performed at the NICU.

3.6. Conclusions

Our data showed that measurement errors in pneumotachometers were significantly affected by both flow rate and oxygen concentration. Therefore, it is necessary to calibrate with the actual oxygen concentrations and flow rates before starting a measurement in clinical or experimental settings. However, frequent calibration procedures during changes in gas composition in the clinical setting is often not practical, e.g. in case of increasing oxygen need in the neonate. For this reason we calculated regression equations to correct flow readings during changing conditions, which significantly reduced the measurement errors.
This means that after a calibration at 0 and 3 L/min and 60 per cent oxygen reliable flow measurements can be achieved in the appropriate flow range and at all oxygen concentrations with the described neonatal pneumotachometers. In practice quick corrections can be performed using polynomials as shown in Figure 4. Further investigation is needed to extend the applicability of the correction factors in humidified and warmed conditions.