Room temperature influences outputs from the Wright jet nebulizer

J. Kongerud**, V. Søyseth**, B. Johansen*

ABSTRACT: Standardization of the solute output from the Wright nebulizer is necessary in nonspecific bronchial challenge to obtain reproducible results. Airflow and driving pressure are known determinants of the output. In an epidemiological study, in which day-to-day variations in room temperature occurred, we found the reproducibility of the output from a Wright nebulizer to be outside the range of acceptance. We have, therefore, examined to what extent ambient temperature and humidity might influence the output from three Wright nebulizers. The solute output was linearly correlated not only to airflow ($r=0.90$) and driving pressure ($r=0.90$) but also to room temperature ($r=0.96$). The mean output increased approximately 23% when room temperature was increased from 19 to 24°C. This is equivalent to an increase in airflow of more than one litre. Ambient humidity did not influence the nebulizer output. When temperature was included in the calibration procedure, the coefficient of variation of the output decreased from 5 to 2%. This emphasizes the need for calibration of the Wright nebulizer with regard to ambient temperature as well as to airflow and pressure, especially in epidemiological field studies in which large variations of temperature are likely to occur.

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Careful standardization of the bronchial challenge test is required to achieve reproducible results that are comparable over time and from laboratory to laboratory. In 1983 the working group “Bronchial Hyperreactivity” of SEPCR (European Society of Clinical Respiratory Physiology) published guidelines for standardization of bronchial challenge with (nonspecific) bronchokonstricting agents [1]. According to this report, both inspired dose and particle size are important determinants of the response to the challenge. One of the recommended methods is that proposed by Cockcroft et al. [2]. The aerosol is generated continuously by a Wright nebulizer and inhaled by tidal breathing over 2 min. Particle size and output from the nebulizer are dependent on the driving pressure and flow, the latter being the more important [3, 4].

In a prospective, epidemiological study of bronchial responsiveness in aluminum potroom workers, we observed large day-to-day variabilities in the output from the nebulizers (unpublished observations). One of the factors that varied was room temperature. At the onset of the challenge, flow and pressure were adjusted manually from zero to the required values. The time to reach these values may also vary and influence the output.

The aim of the present study was to investigate the influence of ambient temperature on nebulizer output. The possible effect on reproducibility of the output of a valve inserted between the manometer and the flowmeter was also examined. The effect of the valve was to produce a square-wave of flow and pressure.

Methods

Three Wright nebulizers (Aerosol Products Ltd), each filled with 3 ml isotonic saline at room temperature, were tested. They were driven by compressed air at ambient temperature and humidity. The latter varied between 40 and 45% during the test period. Airflow was measured by a calibrated flowmeter (Fisher & Porters mod. 10A-3200) at the inlet of the nebulizer. The pressure delivered to the flowmeter (inlet pressure) was regulated by a manometer (Drägerwerk AG Lübek). Figure 1 shows the experimental set-up including the valve between the manometer and the flowmeter.

The nebulizers were weighed on a Sartorius balance. Solute output, determined as the difference in weight before and after exactly 2 min of nebulization, was taken as the arithmetic mean of, usually, ten measurements at each test condition.

To obtain an output of 0.13 mg·min$^{-1}$ at a constant inlet pressure of 3.5·10$^3$ kPa, as recommended by Cockcroft et al. [2], we initially calibrated each nebulizer at 22°C by adjusting airflow. Output was...
determined at several airflows, and the flow needed to give an output of exactly 0.13 mg·min⁻¹ (8.6 l·min⁻¹) was estimated by interpolation.

At constant temperature and pressure, output as a function of flow fits a linear regression model, the correlation coefficient being 0.99, 0.99 and 0.98 for the three devices, respectively (table 2).

Table 2. - Relationship between output and airflow described by simple linear regression (output=a+b·flow) at constant inlet pressure and temperature

<table>
<thead>
<tr>
<th>Neb</th>
<th>a</th>
<th>s.e (a)</th>
<th>b</th>
<th>s.e (b)</th>
<th>r</th>
<th>n</th>
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</thead>
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<td>0.0343</td>
<td>0.0020</td>
<td>0.98</td>
<td>15</td>
</tr>
</tbody>
</table>

Neb: nebulizer; a: intercept; b: regression coefficient; s.e: standard error; r: correlation coefficient.

The regression equations with solute output as the dependent and inlet pressure as the independent variable are shown in table 3. For all three nebulizers a close correlation was found between output and inlet pressure with r=0.89, 0.87, and 0.94, respectively.

Table 3. - Relationship between output and inlet pressure described by simple linear regression (output=a+b·pressure) at constant airflow and temperature

<table>
<thead>
<tr>
<th>Neb</th>
<th>a</th>
<th>s.e (a)</th>
<th>b</th>
<th>s.e (b)</th>
<th>r</th>
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<td>30</td>
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</tbody>
</table>

Abbreviations as in table 2.

The close relationship (r=0.95, 0.99, 0.95) between room temperature and output is given by the regression equations in table 4. The combined effect on output of temperature flow is shown in table 5. An increase in temperature from 19 to 24°C at a constant flow of 8.6 l·min⁻¹ increased output per minute of nebulizer 1 from 0.111 to 0.136 mg (23%). After temperature correction, the coefficient of variation of the measurements decreased from 5 to 2%. Variations in ambient humidity had a negligible effect on temperature (table 6).

Table 4. - Relationship between output and temperature described by simple linear regression (output=a+b·temperature) at constant airflow and inlet pressure

<table>
<thead>
<tr>
<th>Neb</th>
<th>a</th>
<th>s.e (a)</th>
<th>b</th>
<th>s.e (b)</th>
<th>r</th>
<th>n</th>
</tr>
</thead>
<tbody>
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<td>0.0110</td>
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<td>0.0006</td>
<td>0.95</td>
<td>40</td>
</tr>
</tbody>
</table>

Abbreviations as in table 2.
The close correlation between airflow or driving pressure but is also closely correlated to room temperature.  

As nonspecific bronchial provocation testing was developed, many centers elaborated their own methods of bronchial challenge. It became apparent that, unless these methods were standardized, no reliance could be placed on the results and that data from different centers could not be compared. The "Working group on bronchial hyperreactivity" of the European Society for Clinical Respiratory Physiology (SEPCR) made their recommendations for standardization of bronchial challenge tests [1], pointing out that the inspired dose is an important determinant of the response to bronchial challenge. The close correlation between airflow or driving pressure across a jet nebulizer and output has been reported by several authors [4, 6-8], whilst less attention has been paid to ambient temperature and humidity.

Reproducibility of the output from jet nebulizers, including Wright nebulizers, has been thoroughly studied [3, 7, 9]. A difference of approximately 20% has been shown to exist between the highest and lowest outputs for different nebulizers of the same type [6]. In our study the difference in output was less than 1% between the three nebulizers. This small difference may occur by chance or indicate a high quality production of the nebulizers.

From the data in a study by Ryan et al. [3], we have estimated the coefficient of variation for a particular nebulizer to be 4.4%. If temperature was not included in our calibration procedure, the coefficient of variation of the output was 5%. This decreased to 2% when room temperature was corrected. The latter value is lower than that reported by Ryan et al. [3] and considerably lower than the 6.9% intra-nebulizer variation of a hand driven nebulizer recommended for epidemiological studies [10].

The output of jet nebulizers as a function of the airflow rate has been reported to follow a linear model [6], but this finding has not regularly been reproduced by others [11]. Our study confirms that the output is a function of airflow rate and that a linear regression model fits well in the present range. A linear relationship between solute output and ambient pressure was also found. Stein et al. have shown that increase of driving pressure across the nebulizer increases the output [4, 7]. Although we did not measure the driving pressure, defined as the difference between inlet and outlet pressure of the nebulizer, it is reasonable to assume that an increase of inlet pressure of the flowmeter increases the driving pressure. An increase in output due to changes of driving pressure is possibly caused by a change in the size distribution of particles. Since bronchial responsiveness is related not only to the dose deposited in the airways, but also to the distribution of the aerosol in the airways, it is of importance that the driving pressure is kept constant to give both reproducible output and particle size. The physical basis for the effect of temperature on solute output is unclear. At constant room temperature, Hall [12] showed that an increase in temperature of the solution in the vial from 4 to 24°C increased the nebulizer output by approximately 13%. Our study shows that ambient temperature seems to be even more important as we found a 23% increase in nebulizer output when ambient temperature rose by 5°C. Solute output has been reported to be a function of both particle concentration and particle size [4]. As the size of the droplets generated by a nebulizer varies with temperature of the surrounding air [7], changes in particle size, particle number, or both might be a plausible explanation for the variation in output with varying temperatures. This may partly be due to a change in surface tension of the solution, as an increase in solution temperature will diminish surface tension so that smaller droplets are more easily generated.

Our flowmeter is calibrated at 20°C. When temperature increases, flow delivered by the system might

Table 5. - Effect of temperature (°C) and flow \( \text{m}^3/\text{min} \) on solute output described by multiple linear regression (output=a+b·temperature+c·flow) at constant airflow, temperature and inlet pressure

<table>
<thead>
<tr>
<th>Neb</th>
<th>a</th>
<th>SE (a)</th>
<th>b</th>
<th>SE (b)</th>
<th>c</th>
<th>SE (c)</th>
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<td>0.0446</td>
<td>0.0027</td>
<td>0.90</td>
<td>65</td>
</tr>
</tbody>
</table>

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Table 6. - Relationship between solute output and ambient humidity described by simple linear regression (output=a+b·humidity) at constant airflow, temperature and inlet pressure

<table>
<thead>
<tr>
<th>Neb</th>
<th>a</th>
<th>SE (a)</th>
<th>b</th>
<th>SE (b)</th>
<th>r</th>
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</table>

The first output from each nebulizer on each day in the test period was significantly larger than the following, mean output being 0.272 mg and 0.256 mg over 2 min, respectively (se of the difference=0.004 mg, p<0.001).

Insertion of the valve between the air cylinder and flowmeter did not change the mean output or its standard deviation.

Discussion

This study has shown that the output from the Wright nebulizer is not only dependent on flow and driving pressure but also closely correlated with room temperature.

As nonspecific bronchial provocation testing was developed, many centers elaborated their own methods of bronchial challenge. It became apparent that, unless these methods were standardized, no reliance could be placed on the results and that data from different centers could not be compared. The "Working group on bronchial hyperreactivity" of the European Society for Clinical Respiratory Physiology (SEPCR) made their recommendations for standardization of bronchial challenge tests [1], pointing out that the inspired dose is an important determinant of the response to bronchial challenge. The close correlation between airflow or driving pressure across a jet nebulizer and output has been reported by several authors [4, 6-8], whilst less attention has been paid to ambient temperature and humidity.

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increase as well even if the scalar value of the flowmeter is kept constant. According to the manufacturer, however, flow decreases approximately 1% when temperature increases from 20 to 24°C. The effect of temperature on solute output can, therefore, hardly be explained by a change in the delivered flow.

Particle size of an aerosol is also dependent on humidity [13]. The humidity within the nebulizer is presumably independent of ambient humidity. Variations in the latter should, therefore, not influence the output. This assumption is supported by our failure to demonstrate any effect on solute output when ambient humidity varied.

The phenomenon of the first output each day being significantly greater than the following may also be explained by a temperature effect. Prior to the first experiment each day the temperature of the nebulizer equals room temperature. Due to heat loss caused by the first nebulization, the temperature of the nebulizer may decrease substantially, resulting in lower outputs for the second and subsequent nebulizations.

The insertion of a valve between the pressure source and the flowmeter did not improve the reproducibility of solute output. However, a practical benefit was obtained by using the valve, allowing an immediate operation of the system by turning a handle rather than turning the wheels on the rotameter and the pressure gauge.

We have, in the present study, shown that ambient temperature influences the output from Wright nebulizers. A temperature increase of four degrees corresponds to an increase in airflow of one litre. The effect of temperature can not be explained by variations in ambient humidity or airflow delivered to the nebulizer. The calibration procedure must, therefore, include temperature in addition to previous known determinants of the solute output. Calibration of nebulizers is time consuming and not usually a daily procedure. In laboratories where ambient temperature is stable, recalibration at intervals of months is recommended, although the output had been found to remain the same over periods of up to 1.5 yrs (F.E. Hargreave, personal communications). In epidemiological field studies, in which ambient temperature may vary by several degrees over time, frequent calibration with respect to temperature is necessary.

References