Output characteristics of DeVilbiss No. 40 hand-held jet nebulizers

K.N. Chan, M.M. Clay, M. Silverman


ABSTRACT: DeVilbiss No. 40 hand-held nebulizers are widely used for quantifying airway responsiveness in large populations using pharmacological agents. Within each device, the aerosol output and droplet size were reasonably stable over a wide range of bulb pressures, although there were considerable differences in output characteristics between nebulizers. The droplet size was very large compared to conventional aerosol delivery systems, with a mass median diameter greater than 10 μm for three of the five devices. Between 28–50% of the output was in particles sufficiently small for airway deposition (<6.2 μm). A more vigorous compression of the bulb caused a small increase output and a reduction in droplet size, resulting in a much bigger variation in the output of the respirable aerosol (<6.2 μm) with changes in bulb pressure. The loss due to evaporation was about 3.5%, causing a similar rise in the osmolality of the nebulizer solution. In view of the variable nebulizer output and the marked between-operator variation in bulb pressure, the characteristics of Individual DeVilbiss No. 40 nebulizers should be evaluated by individual operators before use in clinical practice or research.

Many clinical and research studies have used inhalation challenge with pharmacological agents to quantify airway responsiveness. A number of different aerosol delivery systems are available, most of which require either a high flow of driving gas or an electrical device to atomize the liquid. Such equipment is often impractical for large population studies or research work outside the laboratory.

Recently YAN et al. [1] have re-introduced the simple, hand-held DeVilbiss No. 40 glass nebulizer as a dosimetric, aerosol delivery system. The driving gas is provided by giving the plastic bulb of the equipment a firm squeeze. This forces air through a narrow nozzle placed just above the orifice of a feedtube. Liquid is drawn up the feedtube by the Bernoulli effect and is shattered into droplets by the rapidly expanding gas. Large droplets are removed by impaction onto the curved throat tube which functions as a baffle. Based on a simple protocol, airway responsiveness to inhaled pharmacological agents can be determined using the DeVilbiss No. 40 nebulizer in 10–15 min. Reproducibility has been found to compare well and results to correlate closely with other standard airway provocation tests [1, 2]. The portability of the equipment and the brevity of the protocol makes the technique ideal for large scale epidemiological surveys. Within the last few years, a large volume of literature has accumulated reporting the distribution of airway responsiveness measured by Yan’s technique, in populations of children and adults [3–7].

The dose and distribution of aerosol in the lung is determined by a large number of factors. The output, size distribution and the physical properties of the droplets, as well as the ventilatory conditions of the subject, could all be important [8]. However, in most studies, assessment of the aerosol droplet size has not been undertaken. Many investigators have taken comfort from the work of RYAN et al. [9], based on seven asthmatic subjects, which suggested that the nebulizer output, but not the aerosol particle size was an important determinant of the outcome of aerosol provocation.

Population studies generally require several operators. As the driving pressure of DeVilbiss No. 40 nebulizers is generated by manual compression of the plastic bulb, it is unclear to what extent the quantity and quality of their output can be influenced by individual differences in the firmness of the squeeze. Wide variation in droplet properties could call into question the suitability of the technique. Our study aimed to examine these important issues.
Methods

Five DeVilbiss No. 40 glass nebulizers (DeVilbiss Inc. Somerset, PA) were examined. In order to monitor the changes in bulb pressure during manual compression, an aneroid pressure gauge (Accoson 0230, A.C. Cossor & Son Ltd, London) with a range 0–450 mmHg (0–60 kPa) was connected to the nebulizer system using a small T-piece and a 5 cm length of rigid, 5 mm tube. Except for measuring droplet size, which required consecutive activations, a control valve (Accoson 1500, A.C. Cossor & Son Ltd, London) was placed at the pressure gauge arm of the system (fig. 1). The latter was used to facilitate measurement of bulb pressure.

In preliminary observations, we had found that there was considerable variation in bulb pressure between nebulizers. The mean bulb pressure of a firm squeeze was about 300±46.5 mmHg (40±6 kPa), ranging from about 250–340 mmHg (33±45 kPa), between nebulizers. There was also a fairly small intra-operator, but marked inter-operator, variation in bulb pressure (coefficient of variation due to differences in the internal volume of the plastic bulbs, the same set-up together with the same nebulizers. The mean bulb pressure of a firm squeeze was about 453±67 mmHg (65±9 kPa), ranging from 375–530 mmHg (50±75 kPa), between nebulizers. The mean bulb pressure of a firm squeeze was about 453±67 mmHg (65±9 kPa), ranging from 375–530 mmHg (50±75 kPa), between nebulizers.

Fig. 1. – System used for measurement of nebulizer output. The nebulizer vent was open only during puffing for output and droplet size measurement. The control valve was removed to allow rapid activation for droplet size measurement.

Output measurements

The measurement of aerosol output was made according to the protocol described by YAN et al. [1]. The weight of the nebulizer, together with 1 ml of normal saline placed in the glass chamber was recorded before and after ten discharges. The procedure was repeated ten times for each nebulizer at each of the above pressures. Measurement of output after single activations was also made at a bulb pressure of 300 mmHg (40 kPa), as weighing after ten puffs would underestimate the variability per puff. The procedure was also repeated ten times for each of the nebulizers. All weighings were carried out on a Sartorius balance, accurate to four figures (Model No. 2605, Sartorius-Werke A.G., Gottingen) at room temperature and humidity.

Droplet size measurements

The size distribution of the aerosol was determined using a Malvern 2600 laser particle sizer (Malvern Instruments, Malvern). One ml of sterile water was placed in the glass chamber of each nebulizer. Sterile water was used because droplets with salt content might have been liable to hygroscopic changes. The nebulizer was then clamped in such a position that the discharge from the exit tube would pass through the laser beam of the particle sizer. The orifice of the tube was 1 cm from the beam, with adequate venting of aerosol by a suction pump. The control valve was removed to facilitate activations in quick successions. For each nebulizer and at each of the above bulb pressures, three determinations of particle size were made. The data were fed into and analysed by a digital computer which had been programmed to sample 10–12 successive activations. The particle size distribution was presented as percentage of total mass in each of 32 size bands as well as in cumulative mass below each size band. The droplet size of the nebulizer output was expressed as mass median diameter (MMD). This was defined as the droplet diameter which divided the total mass equally by size. The dispersion of the droplet size was expressed as the geometric standard deviation (GSD) which was calculated from the ratio between 84.1 and 50% cumulative mass diameters [10].

Table 1. – Output of DeVilbiss No. 40 nebulizers at a bulb pressure of 300 mmHg (40 kPa) determined by single puffs and by batches of ten puffs

<table>
<thead>
<tr>
<th>Nebulizer</th>
<th>Output per puff (based on single puffs)</th>
<th>Output per 10 puffs (based on batches of 10 puffs)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean mg (sd) mg</td>
<td>Mean mg (sd) mg</td>
</tr>
<tr>
<td>1</td>
<td>3.5 (1.28)</td>
<td>14.3 (0.9)</td>
</tr>
<tr>
<td>2</td>
<td>4.7 (1.25)</td>
<td>23.7 (1.4)</td>
</tr>
<tr>
<td>3</td>
<td>4.0 (1.86)</td>
<td>28.4 (0.8)</td>
</tr>
<tr>
<td>4</td>
<td>5.0 (1.35)</td>
<td>29.8 (0.5)</td>
</tr>
<tr>
<td>5</td>
<td>5.3 (1.20)</td>
<td>30.7 (0.7)</td>
</tr>
</tbody>
</table>

Measurements of loss due to evaporation

Evaporative water loss was estimated by measuring the change in solute content following a series of puffs, using the concentration of sodium ions as the marker.
Table 2. - Particle characteristics of DeVilbiss No. 40 nebulizers at a bulb pressure of 300 mmHg (40 kPa) based on triplicate determinations

<table>
<thead>
<tr>
<th>Nebulizer</th>
<th>MMD μm</th>
<th>GSD</th>
<th>Size distribution</th>
<th>Output in droplets of &lt;6.2 μm %</th>
<th>Mean (sd)</th>
<th>Output per 10 puffs in droplets of &lt;6.2 μm mg*</th>
<th>Mean (sd)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.25 (0.37)</td>
<td>10.86 (0.11)</td>
<td>bimodal</td>
<td>50.0 (1.87)</td>
<td>7.1 (0.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>10.90 (0.19)</td>
<td>2.20 (0.03)</td>
<td>unimodal</td>
<td>30.8 (0.32)</td>
<td>7.3 (0.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>12.01 (0.07)</td>
<td>2.39 (0.02)</td>
<td>unimodal</td>
<td>27.6 (0.40)</td>
<td>7.8 (0.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>10.96 (0.18)</td>
<td>2.33 (0.01)</td>
<td>unimodal</td>
<td>29.9 (0.47)</td>
<td>8.9 (0.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>8.56 (0.12)</td>
<td>2.72 (0.01)</td>
<td>unimodal</td>
<td>38.2 (0.10)</td>
<td>11.7 (0.4)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MMD: mass median diameter; GSD: geometric standard deviation; *: based on 10 batches of 10 determinations.

This was done in conjunction with measurement of the output of the nebulizers. The dry weight of each nebulizer was first determined. Two ml of normal saline were placed in the glass chamber, from which 1 ml was withdrawn for measurement of sodium concentration. The weight of the loaded nebulizer was determined before and after 100 manual compressions of the bulb. The change in sodium concentration within the nebulizer was measured using a flame photometer (Model IL343, Instrumentation Laboratory, Warrington). From the change in weight and change in sodium concentration, the evaporative water loss was calculated.

All of the above studies were carried out under conditions of room temperature and pressure.

Results

The output characteristics for the five hand-held nebulizers at a typical bulb pressure of 300 mmHg (40 kPa) are summarized in table 1. The within operator variability of the bulb pressure at this target pressure was about 7%. The output per puff measured after single activations was considerably higher than the average after ten puffs. Determination of output after ten puffs reduced both the evaporative water loss due to corking and uncorking of the nebulizer as well as measurement error, but it must underestimate the variability per puff. For this reason, calculation of output was based on measurements done after batches of ten puffs. The range and the standard deviation of output based on measurements done after ten puffs were similar to those reported by Yan et al. [1] except for one nebulizer (nebulizer 1) with a smaller output and significantly different bimodal droplet size distribution from the rest of the nebulizers. The size distribution of all other nebulizers was unimodal. There was no visually detectable difference between this and the other nebulizers. On the whole, the repeatability of the output measured after ten puffs was much better than that after single puffs.

The MMD was very large (6.2-12 μm) compared to standard aerosol-delivery systems, with a GSD in excess of 2 (table 2). Because droplets with a MMD >6 μm have been considered too large to penetrate the tracheobronchial tree [11], the percentage and the mass of output which fell in the particle range <6.2 μm was

Fig. 2. - Output per 10 puffs, mass median diameter of aerosol discharge and output of particles of size <6.2 μm per 10 puffs of the five DeVilbiss No. 40 nebulizers in relation to peak bulb pressure. Each value of output is the mean of 10 batches of 10 activations and each value of mass median diameter is the mean of three separate determinations of droplet size. Error bars are not shown, since variation was extremely small (table 1).
calculated. Between 28-50% of the total output was below this size.

With increasing firmness of squeeze and hence with increasing bulb pressure, all five nebulizers showed an increase in output and a decrease in MMD (fig. 2). Taken together, an increase in bulb pressure by 100 mmHg (13 kPa) from 250 mmHg to 350 mmHg resulted in a mean increase in output by 12.3% (range 9.7-21.6%) and a mean fall in MMD by 12.8% (range 4.9-25.7%). Consequently there was a bigger increase in the output of respirable particles of size <6.2 μm over this range of bulb pressures (mean increase 31.4%, range 26.0-36.3%). With the exception of nebulizer 1 which showed a marked increase in osd by 9.8%, there was no significant change in osd with bulb pressure.

The evaporative water loss was 3.5±0.57% of the total nebulizer output. With an initial fill of 1 ml, the sodium ion concentration in the saline solution increased by an average of 5 mmol/l after 100 puffs.

Discussion

Although a number of studies of airway responsiveness in large populations have been based on the DeVilbiss No. 40 jet nebulizer, the characteristics of the aerosol generated by this hand-held equipment have not been reported in detail. This information could be very important, since different operators prefer to adjust for the known variations in output in different ways. Some only choose jets with an output of 2.5-3.5 mg per puff [12], whilst others adjust the concentration of methacholine or histamine to allow for differences in output [13]. Neither technique is entirely satisfactory, as there may be considerable between-operator variation in bulb pressures in addition to variation of output between nebulizers.

In preliminary studies using the same nebulizer system, we found that different operators produced widely varying bulb pressures, depending on the degree of firmness with which the nebulizer bulb was squeezed. Our study was somewhat reassuring in that, with a single operator and provided a reasonably firm squeeze was made, i.e. with a bulb pressure between 250-350 mmHg (33-47 kPa), the variation in output and droplet size of each nebulizer with bulb pressure was fairly consistent.

There were considerable differences between nebulizers in both the output and size distribution of droplets. The MMD of the droplets could not be predicted by the mass of their output. The changes in both output and MMD with changes in bulb pressure occurred largely in parallel between nebulizers, suggesting that although the overall output characteristics of each nebulizer were distinct, each responded similarly to increasing bulb pressures.

The droplet size of DeVilbiss No. 40 nebulizers was much larger than for other conventional aerosol delivery systems. For instance, the MMD of the Wright and DeVilbiss 646 jet nebulizers are reported as 1.2 and 2.6 μm, respectively, at a gas flow rate of 6-8 l/min [9]. As droplets with a diameter >6 μm are probably too large for deposition in the lower airways [14, 15], it is clear that the majority of the output of the DeVilbiss No. 40 will be deposited in the mouth or oropharynx. Not surprisingly, transient throat symptoms were common in one survey of children, using histamine as the agent [12]. The proportion of aerosol capable of deposition in the bronchial tree was 50% or less of the total output, although the respirable output increased with increasing bulb pressure.

Moreover, there was some evaporative water loss. It caused a rise of about 3% in the concentration of the nebulizer after 100 puffs, with a 1 ml starting volume. In clinical use, the nebulizer should be refilled after no more than 100 puffs and kept corked when not in use.

The much larger MMD of aerosol produced by the hand-held nebulizer compared to other conventional jet nebulizers means that the pattern of airway deposition of inhalant is likely to be very different. Consequently, the results obtained by this technique might not necessarily be equivalent to those reported for other established methods. In clinical studies, therefore, a valid conclusion can only be drawn by reference to a comparable control group. For epidemiological studies, it may be impossible to compare the prevalence of airway responsiveness between populations ascertained using different equipment with diverse differences in aerosol output and droplet characteristics. At the very least, this study suggests that differences between DeVilbiss No. 40 nebulizers should be assessed before starting a project. Either a set should be obtained with matched characteristics, or the challenge protocol should be amended to compensate for differences in output [7]. For studies involving more than one operator, because of the marked between-operator variability in bulb pressure and hence output, nebulizer output for individual operators should also be assessed.

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References


RÉSUMÉ : Les nébulisateurs DeVilbiss No. 40 à propulsion manuelle sont utilisés largement pour quantifier la réactivité des voies aériennes dans des grandes populations au moyen d’agents pharmacologiques. Nous avons examiné les caractéristiques des aérosols provenant de cinq de ces nébulisateurs. Pour chacun des nébulisateurs, la production d’aérosol est la taille des particules était raisonnablement stables dans un large éventail de pressions sur la poire, qu’où qu’il y ait des différences considérables des caractéristiques de production entre les divers nébulisateurs. La taille des particules est très grande par comparaison aux systèmes de production d’aérosols conventionnels, le diamètre médian de masse étant supérieur à 10 μm pour 3 des 5 appareils. De 28 à 50% seulement de la production existent sous forme de particules suffisamment petites pour permettre un dépôt au niveau des voies aériennes (<6.2 μm). Une compression plus vigoureuse de la poire provoque une légère augmentation de la production et une réduction de la taille des gouttelettes, entraînant une beaucoup plus grande variation de la production d’aérosols respirables (<6.2 μm) en cas de modification de la pression sur la poire. La perte due à l’évaporation est de l’ordre de 3.5%, ce qui entraîne une augmentation parallèle de l’osmolalité de la solution nébulisée. En raison de la production variable des nébulisateurs et des variations marquées entre opérateurs en ce qui concerne la pression sur la poire, les caractéristiques des nébulisateurs DeVilbiss 40 individuels devraient être évaluées par les utilisateurs individuels avant leur utilisation en pratique clinique ou pour la recherche. Eur Respir J, 1990, 3, 1197–1201.