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TECHNICAL NOTE

Comparison of twenty three nebulizer/compressor combinations for domiciliary use

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Comparison of twenty three nebulizer/compressor combinations for domiciliary use. E.C. Smith, J. Denyer, A.H. Kendrick. ©ERS Journals Ltd 1995.

ABSTRACT: We have assessed the physical and dynamic characteristics of 23 home jet nebulizer/compressor combinations currently available in the UK and Europe.

The combinations were evaluated in terms of pressure-flow characteristics, aerosol mass distribution, volume output, electrical costs, and sound level. In addition, we determined the effect of nebulizer fill volume on aerosol mass distribution and volume output. One nebulizer was used with six different compressors, and four compressors were tested with three different nebulizers.

The pressure-flow relationships showed a wide variation between models, as did flow-rate at the nebulizer (range 3.0–8.0 L·min^{-1}). The mean±SD volume nebulized after 10 min using an initial fill volume of 2.5 and 5.0 mL was 46±9 and 34±12%, respectively. The mass median aerodynamic diameter (MMAD) over a 5 min nebulization ranged 2.6 to 10.2 µm. Nine of the nebulizations produced an MMAD of less than 5 µm at both fill volumes. Changing nebulizer/compressor combinations affected flow rate, MMAD and volume output. Sound levels varied between models. Running costs were low, with all using less than 74 kilowatt hours of energy per year.

We conclude that there is a wide variation in performance of nebulizer/compressor combinations for use with nebulized bronchodilators. Correct matching of the nebulizer/compressor is seen to be important to ensure optimum performance. We recommend that: 1) manufacturers of nebulizers provide information on the required flow rate at the nebulizer to produce the required MMAD, and the percentage of aerosol/mass contained in particles under 5 µm; and 2) suppliers of nebulizer/compressor systems match the combinations more carefully to achieve optimal delivery of the nebulized drug to the patient, and that users should use recommended combinations.

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Portable nebulizer/compressors are increasingly being used by asthmatics and patients with chronic obstructive airway disease as part of their domiciliary treatment using inhaled β_2-agonist and anticholinergic drugs. Since the last published comparison [1], many new nebulizers have become available, or previous models updated. Furthermore, in the United Kingdom, the National Asthma Campaign (NAC) (London, UK) provides a list of recommended nebulizer/compressor combinations for potential purchasers. Those not on the list are generally regarded as unsuitable. We have compared 23 nebulizer/compressor combinations, some of which are on the list, to determine their physical and dynamic characteristics.

Methods

The manufacturers of all compressors known to the authors were approached and asked to supply a complete system of nebulizer, compressor, tubing, face mask and instruction manual.

Physical characteristics

The maximum dimensions of each compressor were determined using a ruler to the nearest 1.0 mm. Mass was measured using scales (Seca, Model 750) accurate to the nearest 0.1 kg. The sound level (dBC) of each combination was determined at a distance of one metre, using a sound level meter (Dawe Instruments, Type D-1422C), the value obtained being to the nearest 1 dB. The meter was calibrated at a single level of 114 dB at 1 kHz (Dawe Acoustic calibrator D1411E, Dawe Instruments).

Dynamic characteristics

The pressure-flow characteristics were determined using a rotameter (Platon Flow Control, Gapmeter GTLK) and a pressure transducer (Validyne MP45) in series. The transducer was linear over its working range, and the

system was calibrated using a water manometer before each series of experiments. The output of the transducer was displayed on a X-Y recorder (Bryans 26700 Model A4). Free flow was recorded as the maximum flow rate ($L \cdot min^{-1}$) the compressor developed at zero resistance. Maximum static pressure (kPa) was recorded as the maximum pressure that the compressor could develop at zero flow. This was achieved by closing the needle valve of the rotameter fully. A pressure-flow curve was obtained for each combination by adjusting the needle valve of the rotameter to different flow rates, from free flow, to zero flow, and the corresponding pressure recorded.

The pressure and flow-rate generated at the nebulizer were estimated by replacing the flow meter with the nebulizer and recording back pressure using a fill volume of 2.5 and 5.0 mL sterile water. The flow rate corresponding to the measured back pressure was obtained from the pressure-flow curve.

The volume output of the nebulizer was estimated at 2, 5 10, 15 and 20 min for each combination using 2.5 and 5.0 mL starting volume of sterile water. For each assay, the nebulizer was dried and its dry mass recorded to the nearest 0.01 g using scales (Ohaus, CT200), which had a two point calibration performed at regular intervals throughout the studies. The required volume of sterile water was pipetted (Macro Transferpettor) into the nebulizer cup and the mass of the cup plus water recorded. The nebulizer/compressor was then run for the required length of time, at the end of which the mass of the nebulizer cup and water remaining was measured. Estimates of volume output at the different times were made in a random order.

Determination of aerosol mass distribution

The size distribution of the aerosol mass generated by each of the combinations was determined from laser diffraction (Malvern, Master Sizer MS20), the analysis of particle size distribution into the volume distribution being based upon the Mie Theory. The focal length was 100 mm, giving a measurement range of 0.5–170 µm. Prior to use, the laser beam was automatically aligned with the collector and background readings taken, these being subtracted from each of the measurements subsequently made. Each measurement is the average taken of 200 individual measurements made over approximately 5 s. To avoid the effect of fluctuations in natural daylight affecting this background reading, all measurements were made in a darkened room.

Sterile water was used in all studies. The aerosol produced was presented to the laser in a fixed configuration using a specially designed presentation module (Medic-Aid, UK). This ensures that the droplets are carried in such a manner that they are not affected by contact with ambient air, and does not change the particle distribution between the nebulizer and the point at which it is presented to the laser. Since the density of water is essentially 1.0, the volume distribution which the laser produces can be regarded as the mass distribution. Particles were presented to the laser beam in a horizontal mode to reduce the effects of gravity on the measurements.

The nebulizer was filled with 2.5 and 5.0 mL water and nebulized for 5 min. Throughout this nebulization period, the aerosol mass distribution was recorded at 1 min intervals. For two compressors (Aeroneb Standard and Porta-Neb 50) measurements were made over a longer period of 10 min to determine the variation of aerosol mass distribution with time.

From the aerosol mass distribution, as obtained from the laser diffraction measurements, the mass median aerodynamic diameter (MMAD) was obtained. This is the particle diameter about which 50% of the mass of the aerosol particles is distributed. The percentage of aerosol mass less than 5 µm was also obtained from this plot.

Yearly electrical costs

The yearly electrical costs of the compressor were calculated on the basis of four 15 min nebulizations daily for one year. The power rating (Watts) of the compressor was used to calculate the energy consumed (kilowatt hours) for nebulization.

Different nebulizer/compressor combinations

Four compressor units were each supplied with three different nebulizer units. For each combination, the above measurements were made to compare any differences in performance. Performance differences were also compared for one nebulizer (Cirrus) that was available with six different compressors.

Data analysis

Comparison of measurements at different times was made using paired t-tests, whilst to compare the variation in MMAD over time, analysis of variance (ANOVA) was used. Linear regression and ANOVA as applied to regression was used to determine relationships between a number of measurements. To compare equations obtained at different fill volumes, analysis of covariance was used to assess any differences in slope and intercept. Results are given as mean±SD.

Results

Physical characteristics

The physical characteristics of the compressors, the nebulizer chambers supplied, and estimated annual energy consumption are given in table 1. The overall dimensions, mass, sound level and energy consumption varied between models, two of which were multivolt (Medix Traveller and AFP TO1).

Dynamic characteristics

The pressure-flow characteristics of the compressors showed a wide range both of maximum static pressure

Table 1. – Compressors, nebulizers, their mass, dimension, sound level, and units of electricity comsumed per year

No.	Compressor	Nebulizer	UK supplier	Mass kg	Dimensions H×D×W mm	Sound level dB	Energy consumed kW·h^{-1}	NAC listed
1	Aquillon	A) Neb MKII B) Ava Neb 1780 C) Hudson		3.3	125×170×230	65	30.5	No
2	Pari Inhalierboy	Own	Pari	2.9	95×160×205	59	43.8	No
3	Aeroneb Standard	A) Cirrus B) Cirrus C) Italian	Deva Medical	2.1	115×190×250	63	32.8	No
4	Aeroneb High Power	A) Cirrus B) Own C) Italian	Deva Medical	2.1	115×190×250	63	32.8	No
5	Porta-Neb 50	Acorn	Medic Aid	3.0	100×350×225	61	73.0	Yes
6	Atomolette	Own	Sinclair Medical	2.5	235×175×160	50	51.3	Yes
7	Medix 2000	Cirrus	Medix	3.0	120×375×240	62	25.6	Yes
8	Medix Traveller	Cirrus	Medix	4.1	120×375×240	68	16.4	Yes
9	Medix Minor	Cirrus	Medix	3.2	155×210×245	65	16.4	No
10	Pulmo-Aide	Own	DeVilbiss	3.1	200×260×240	67	38.3	Yes
11	Nebu Pump	Acorn		3.3	135×165×235	63	18.1	No
12	AFP NO1	Microneb	AFP Medical	2.9	95×345×215	62	54.7	Yes
13	AFP TO1	Microneb	AFP Medical	3.0	95×345×215	60	10.9	Yes
14	Inspiron	Minineb	AAH Medical	3.1	115×140×240	65	32.8	No
15	Novair II	A) Microcirrus B) Hudson C) Cirrus	Intersugical	4.9	96×155×200	63	32.0	Yes

UK suppliers are either the manufacturer of the compressor or are UK agents. Nebulizer: "Own" is made by the compressor supplier. H: height; D: depth; W: width. NAC listed: compressor listed by the National Asthma Campaign, UK.

Table 2. – Pressure and flow rate at the nebulizer, the MMAD and the percentage of particles less than 5.0 µm at a fill volume of 2.5 and 5.0 µm

Compressor/nebulizer combination		Pressure	Flow rate	2.5 ml fill volume		5.0 ml fill volume	
		kPa	L·min^{-1}	MMAD	% <5.0 µm	MMAD	% <5.0 µm
1A	Aquillon/Neb MKII	185	7.0	2.6	82	2.6	83
1B	Aquillon/Ava Neb 1780	145	8.0	4.3	58	4.0	61
1C	Aqillon/Hudson	132	7.2	4.9	51	5.0	51
2	Pari Inhalierboy/Own	135	4.1	6.5	36	6.2	39
3A	Aeroneb Standard/Cirrus	67	3.9	6.6	35	6.7	35
3B	Aeroneb Standard/Own	59	3.0	10.1	16	9.1	20
3C	Aeroneb Standard/Italian	62	3.6	10.2	21	10.1	22
4A	Aeroneb High Power/Cirrus	104	4.8	7.6	28	7.7	28
4B	Aeroneb High Power/Own	96	3.8	7.5	30	8.4	24
4C	Aeroneb High Power/Italian	99	4.0	10.0	21	9.5	22
5	Porta-Neb 50/Acorn	110	6.2	4.7	54	4.5	56
6	Atmomlette/Own	79	4.2	7.6	28	6.6	36
7	Medix 2000/Cirrus	126	6.8	4.0	61	4.1	61
8	Medix Traveller/Cirrus	126	7.0	4.1	61	4.2	59
9	Medix Minor/Cirrus	104	6.9	3.9	62	4.1	60
10	Pulmo-Aide/Own	113	5.1	5.9	42	6.3	38
11	Nebu Pump/Acorn	90	5.6	4.7	55	5.0	50
12	AFP NO1/Microneb	121	6.2	4.3	59	4.3	58
13	AFP TO1/Microneb	127	6.4	4.3	60	4.3	60
14	Inspiron/Minineb	71	5.7	6.8	35	6.9	35
15A	Novair II/Microcirrus	105	6.7	7.0	39	5.4	48
15B	Novair II/Hudson	90	5.8	6.1	39	6.1	39
15C	Novair II/Cirrus	92	5.8	4.5	57	4.2	59

MMAD: mass median aerodynamic diameter.

Table 3. – Compressors/nebulizer combination showing the volume output at 5, 10 and 20 min for a 2.5 and 5.0 ml fill volume

Compressors/nebulizer combination		Volume output %					
		2.5 ml fill volume			5.0 ml fill volume		
		5 min	10 min	20 min	5 min	10 min	20 min
1A	Aquillon/Neb MKII	50	57	72	27	60	83
1B	Aquillon/Ava Neb 1780	32	48	72	-	-	-
1C	Aqillon/Hudson	25	33	50	24	50	57
2	Pari Inhalierboy/Own	50	64	57	29	71	77
3A	Aeroneb Standard/Cirrus	28	43	49	10	19	28
3B	Aeroneb Standard/Own	14	30	47	8	17	27
3C	Aeroneb Standard/Italian	23	40	48	9	24	40
4A	Aeroneb High Power/Cirrus	34	48	64	10	20	34
4B	Aeroneb High Power/Own	19	38	43	11	22	44
4C	Aeroneb High Power/Italian	37	48	60	19	24	67
5	Porta-Neb 50/Acorn	30	38	66	17	44	68
6	Atmomlette/Own	33	36	52	17	25	62
7	Medix 2000/Cirrus	40	46	68	19	38	66
8	Medix Traveller/Cirrus	37	42	59	16	30	65
9	Medix Minor/Cirrus	32	44	67	17	26	65
10	Pulmo-Aide/Own	26	44	51	16	29	64
11	Nebu Pump/Acorn	30	46	65	16	30	58
12	AFP NO1/Microneb	28	59	72	17	30	64
13	AFP TO1/Microneb	43	66	81	23	42	75
14	Inspiron/Minineb	41	51	56	24	43	69
15A	Novair II/Microcirrus	32	42	50	22	41	62
15B	Novair II/Hudson	34	44	54	23	41	66
15C	Novair II/Cirrus	39	48	58	11	41	63

For combination 1B at the 5.0 ml fill volume, no data were obtained due to persistant leaking.

(range 98–452 kPa) and of free flow (range 7.0–12.1 $L \cdot min^{-1}$). The flow rates and the pressures obtained at the nebulizers are given in table 2. Thirteen combinations had a flow rate at the nebulizer of less than 6 $L \cdot min^{-1}$. Flow rate ($L \cdot min^{-1}$) at the nebulizer, within the range 3.0–8.0 $L \cdot min^{-1}$, was positively correlated to the pressure (kPa) at the nebulizer according to the relationship:

flow rate=2.17+0.03 pressure: (RSD=1.1: r=0.64; p<0.001)

The volume of water output at 5, 10 and 20 min for a fill volume of 2.5 and 5.0 ml is given in table 3. The pattern of output was similar for all combinations with a 2.5 mL fill volume, showing a curvilinear increase up to 20 min. For the 5.0 mL fill volume, the output was more varied than for the 2.5 mL fill volume, with the combinations having low flow rates at the nebulizer performing much worse at this fill volume. For combination 1B, no data were obtained at 5.0 mL fill volume because of persistent leaking. Examples of the relationship of volume output to time are given in figure 1.

The volume output was still increasing at 20 min for both starting volumes. The mean percentage of water

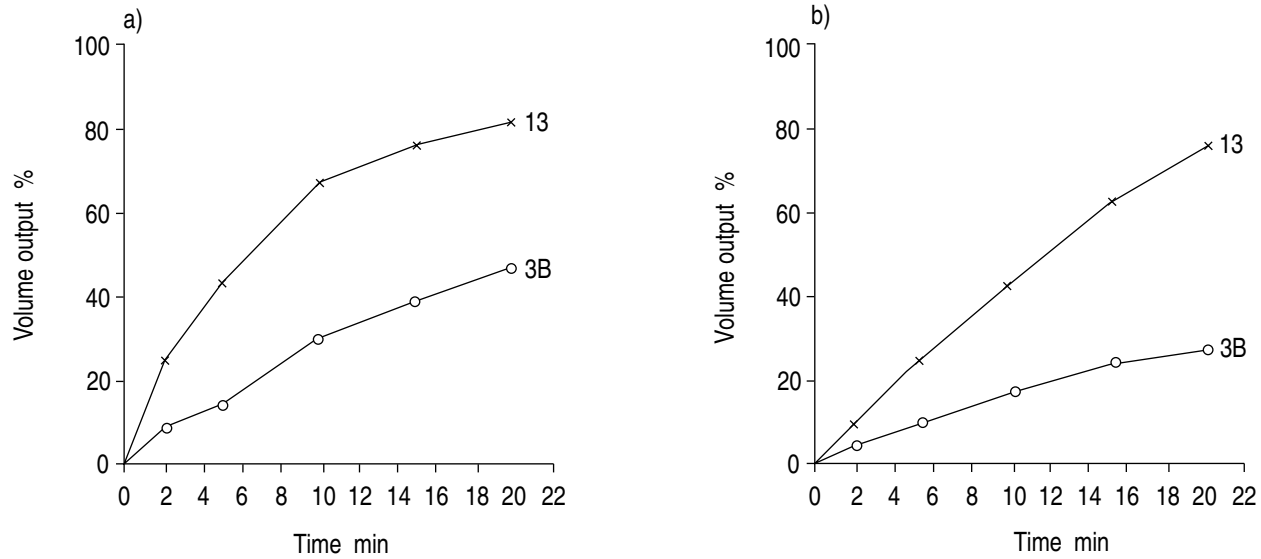

Fig. 1. – Examples of high and low volume output for a fill volume of: a) 2.5 mL; and b) 5.0 mL. Data are given at 2, 5, 10, 15 and 20 min, for compressor nebulizer combinations 3B (—○—) and 13 (—×—). See table 2 for explanation of 3B and 13.

nebulized at 5 and 10 min were 33±9 and 46±9% respectively, for the 2.5 fill volume; and 18±6% and 34±12% respectively, for the 5.0 mL fill volume. Five combinations (1C, 3A, 3B, 3C and 4B) failed to achieve a volume output of greater than 50% at 20 min (table 3). For the remaining combinations, the time needed to achieve a 50% volume output for a 2.5 and a 5.0 mL fill volume was 12.8±4.5 and 14.3±3.1 min respectively, which were not significantly different.

Aerosol mass determination

There was little variation in the MMAD for a 2.5 and 5.0 mL fill volume for the two combinations assessed (fig. 2). The mean MMAD was 9.7 and 9.5 µm with coefficients of variation of 4.8 and 2.8% for combination 3B, and 4.7 and 4.6 µm with coefficients of variation of 1.4 and 0.8% for combination 5, for the 2.5 and 5.0 mL fill volumes, respectively.

The MMAD and the percentage of aerosol mass in particles less than 5.0 µm for each combination at both fill volumes are given in table 2. Nine of the combinations had an MMAD of less than 5.0 µm, at either fill volume. The MMAD (µm) was lower at higher flow rates at the nebulizer, and was inversely correlated to the flow rate ($L \cdot min^{-1}$) at the nebulizer according to the equations:

$MMAD_{2.5}$=13.0 -1.26 flow: (RSD=1.2; r=0.83; p<0.001)
$MMAD_{5.0}$=12.7 -1.23 flow: (RSD=1.0; r=0.86; p<0.001)

Analysis of covariance showed that these equations were not significantly different and, therefore, the relationship of flow rate to MMAD is independent of fill volume. To produce an MMAD of 5.0 µm or less, a flow rate of 6.3 $L \cdot min^{-1}$ at the nebulizer is required.

The percentage of aerosol mass in particles less than 5.0 µm ranged from 16–82% (mean 45%) and 20–83% (mean 45%), respectively, for the two fill volumes, and was independent of the fill volume. However, the percentage of aerosol mass in particles less than 5.0 µm was inversely correlated to the flow rate ($L \cdot min^{-1}$) at the nebulizer according to the equations:

$Percent_{2.5}$=10.2 flow -11.6: (RSD=9.2; r=0.84; p<0.001)
$Percent_{2.5}$= 10.0 flow -10.1: (RSD=8.6; r=0.85; p<0.001)

Each nebulizer/compressor combination produced its own distinctive distribution histogram of particle size, examples of which are shown in figure 3 both for 2.5 and 5.0 mL fill volumes.

Different nebulizer/compressor combinations

The Cirrus nebulizer was available with six different compressors (table 1), whilst four compressors were available, each with three different nebulizers.

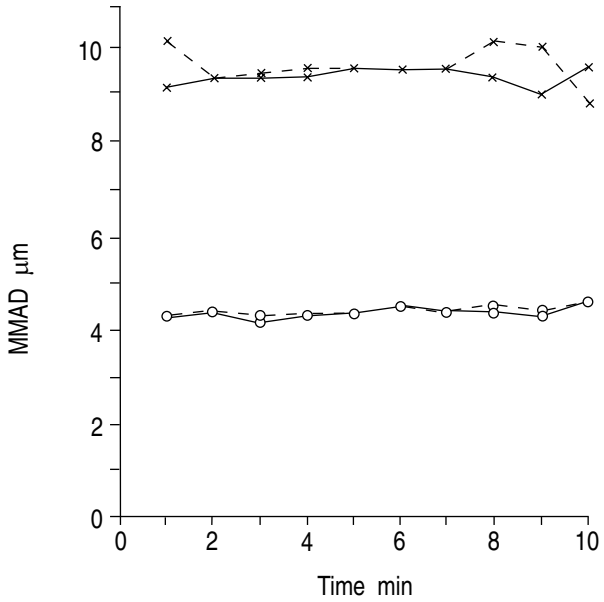

Fig. 2. – Variation over a 10 min nebulization in mass median aerodynamic diameter (MMAD) for the Aeroneb/Own and the Porta-Neb 50 combinations for 2.5 and 5.0 mL fill volumes. —○— : Porta-Neb 50, 2.5 mL fill volume; - -○- - : Porta-Neb 5.0, 50 mL fill volumes; —×— : Aeroneb/Own, 2.5 mL fill volume; - -×- -: Aeroneb/Own, 5.0 mL fill volume.

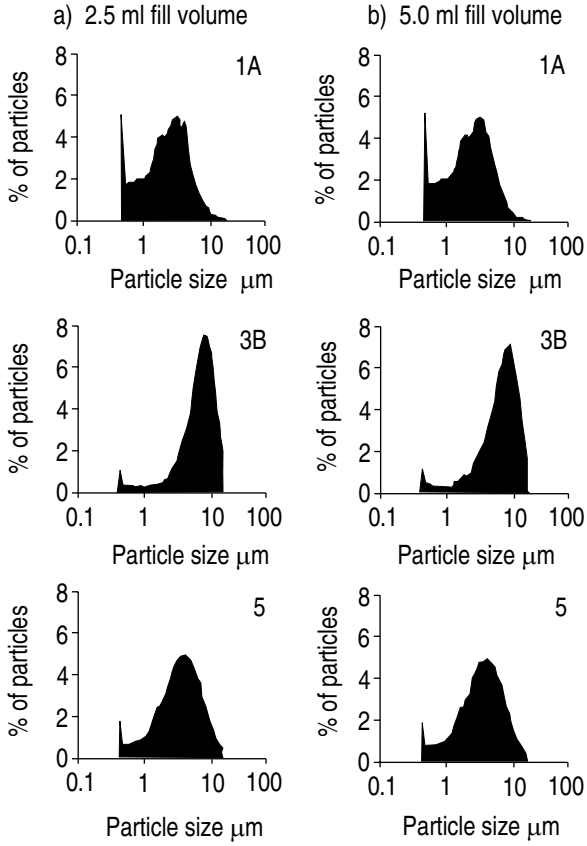

Fig. 3. – Particle size distributions for combinations 1A, 3B and 5. Each histogram represents the percentage of particles against particle size at fill volumes of: a) 2.5; and b) 5.0 mL. The number in the top right hand corner of each histogram refers to the combination number in table 1. The range 0–22.2 µm accounted for approximately 97% of all particles at the 2.5 and 5.0 mL fill volume.

The effect of using different compressors with the Cirrus nebulizer showed a significant relationship between flow rate ($L \cdot min^{-1}$) at the nebulizer and pressure (kPa):

Flow rate=0.91+0.05 pressure: (RSD=0.8; r=0.82; $p<0.05$)

The percentage volume nebulized at 10 min for the 2.5 and 5.0 mL fill volumes ranged from 42–48% (mean 45%) and 19–41% (mean 29%). The MMAD ranged from 3.9–7.7 µm, and was significantly related to the flow rate 9 ($L \cdot min^{-1}$) at the nebulizer for both 2.5 and 5.0 mL fill volumes, the relationships being:

$MMAD_{2.5}$=11.5 -1.1 flow: (RSD=0.8; r=0.85; $p<0.05$)
$MMAD_{5.0}$=11.5 -1.1 flow: (RSD=0.9; r=0.82; $p<0.05$)

The flow rate at the nebulizer was not greatly different for each of the three nebulizers with the four compressors (table 2). The volume output, however, showed marked variations at 5 and 10 min for the combinations for the 2.5 and 5.0 ml volume (table 3), whilst the MMAD showed similar marked variations at the 2.5 and 5.0 ml fill volumes (table 2).

Discussion

This study has investigated 23 compressor/nebulizer combinations that are commercially available to the domiciliary market for the provision of inhaled therapy. The data presented is primarily related to the use of β_2-agonist and anticholinergic drugs and to drugs with similar densities and viscosities. The data are, therefore, not directly applicable to nebulized drugs, such as pentamidine.

Correct use of jet nebulizers depends partly on their design and operation and partly on their use by patients. Of equal importance, for domiciliary use, is the correct matching of compressor and nebulizer, since flow rate at the nebulizer and aerosol mass distribution are dependent on this matching [1]. Therapeutic aerosols such as β_2-agonists and anticholinergics, should ideally have an MMAD of less than 5 µm. However, manufacturers often simply quote a percentage of the total quantity that is smaller than a certain size. If this size is not 5 µm, then without information on the overall distribution of the aerosol, the effective portion of the aerosol cannot be determined. Furthermore, manufacturers often do not quote the required flow rate at the nebulizer which would produce the majority of particles under 5 µm.

Aerosol mass distribution is critically dependent upon the design of the baffle structures which surround the nebulizer orifice [2]. The baffles filter out the large droplets and return them for renebulization, so that any small droplets within the respirable range leave the nebulizer. The operating characteristics of the nebulizer also have an important effect on the size distributions of the aerosols released. Aerosol diameter has been shown to be inversely related to the flow rate of the gas at the nebulizer [3, 4], whilst the rate of aerosol output increases with the flow rate. A high flow rate at the nebulizer should, therefore, allow short patient treatment times, which should enhance patient compliance [5].

From the literature, it appears that the optimal characteristics for nebulizers are a flow rate at the nebulizer of 6–8 $L \cdot min^{-1}$, which will produce aerosols where the majority of the mass is in particles of less than 5 µm, together with a required high aerosol output to maximize patient compliance.

Dynamic characteristics

Pressure and flow. The dynamic characteristics for the 23 combinations varied considerably. Of the 23 combinations, only 10 achieved a nebulizer flow rate of greater than 6.0 $L \cdot min^{-1}$. The relationship between flow rate and MMAD revealed an ideal flow rate of 6.3±1.0 $L \cdot min^{-1}$ to produce an MMAD of 5 µm, suggesting that it would be possible for combinations with lower flow rates to produce an MMAD of less than 5 µm. This was indeed the case for combination 11 and 15C.

Volume output. The volume output was assessed using sterile water rather than a bronchodilator drug. This was mainly for safety reasons, but also for cost. Furthermore, STEVENTON and WILSON [1] had shown similar outputs occurred for water and salbutamol. Although different bronchodilator drugs may achieve different volume outputs, the use of sterile water as a marker of output will provide a guide to the performance of the nebulizer/compressor combination.

The volume output was generally higher at high flow rates. There was a wide variation in the percentage output at 5 and 10 min of nebulization both for 2.5 and 5 mL fill volumes. Some combinations achieved very low volume outputs and the time taken to nebulize 50% of the fill volume varied considerably.

An important distinction must be made between volume output, which is simply the total volume of solution lost from the nebulizer after a period of time, and drug output, which reflects the amount of drug that is released in the same period of time. Nebulizer output, as measured by weighing the nebulizer unit before and after activation does not reflect the actual amount of drug delivered [6–9] because some of the solution will have evaporated. Thus, weight loss is likely to overestimate the aerosol output from any combination. Drug output should be assessed using more appropriate techniques [10].

Despite the limitations of using weight loss, the technique does provide some useful information of the performance of the nebulizer/compressor system. Combinations, such as 3A, 3B and 3C, which have long nebulization times may deter patients from using their nebulizers optimally. These patients may not, therefore, gain optimal benefit from their treatment.

Particle size

To achieve a therapeutic effect, particles of nebulized bronchodilators should have an MMAD of less than 5 µm.

Larger particles (5–100 µm) are principally deposited in the nasopharynx, whilst particles of less than 5 µm will be predominately deposited in the lungs, including alveolar deposition [11–14]. Particles that are less than 0.5 µm will reach the alveolar region with around 15% of the drug delivered being deposited [14]. This is because the method of deposition in the lung is due to gravitational effects, and the small size of the particles means that the time taken for the drug to deposit in any larger quantity is actually longer than the breathing cycle, and, therefore, the majority of the drug will be exhaled again.

Within the range 0 to 5 µm, small changes in particle size do not seem to be of major clinical significance [15, 16]. One study [17] using a single nebulizer has shown that only about 12% of the drug is delivered to the lung, whilst about 1% remains in the mouth. However, it is likely that these values for deposition will differ depending on the nebulizer used. Where particles are greater than 5 µm, greater quantities of the drug will be deposited in the buccal cavity and the nasopharynx [18–21]. To be of use, the particles of nebulized bronchodilators must then be absorbed systematically or swallowed.

We have looked at the variation in the distribution of aerosol mass for all combinations of nebulizer/compressor, using laser diffraction. This method provides a rapid source of data collection and data analysis, when compared to other methods currently available [6, 22]. The specific information provided is that of the MMAD, the percentage of the aerosol mass in particles under 5 µm and the overall distribution scattergram.

In theory, to be effective, the MMAD should be less than 5 µm. In this study, only 10 of the 23 combinations met this criterion, regardless of fill volume. Of more interest were the frequency distribution scattergrams for each combination at the two fill volumes. The median is the central point where half of the points are less than or equal to it and half are greater than or equal to it. Therefore, a distribution in which a large proportion of the mass is below 1.0 µm will influence the MMAD value. Hence, for combination 1B, which had an MMAD of less than 5 µm, about 6% of the mass was in particles of less than 0.5 µm, and approximately 15% of the mass was in particles below 1.05 µm. This will have the effect of distorting the scattergram and, more importantly, of lowering the MMAD. Thus, it is misleading to rely on the MMAD alone. Rather the MMAD should be used with caution and in conjunction with the complete frequency distribution curve. Other information, such as the percentage of the aerosol mass in particles below 5 µm is also misleading for the same reasons as quoting the MMAD. Perhaps the percentage of particles between 3 and 5 µm would be more useful, since this covers the important range of particles for effective lung deposition.

An important observation was that the MMAD was not affected by the fill volume. Fill volume is generally in the range 2.5–5 mL. Often the drug solution is diluted with normal saline. A previous study advocated a minimum fill volume of 4 ml and an airflow rate of 6 $L \cdot min^{-1}$ to optimize nebuliser output [5]. However, recent evidence suggests that this will have the disadvantage of prolonging the nebulization time rather than increasing the amount of drug delivered [23]. The fact that MMAD is independent of fill volume will permit the use of fill volumes of greater than 2.5 mL if required to provide combined drug therapy, such as salbutamol and ipratropium, during a single nebulization. The optimum fill volume will be influenced by the residual volume.

Physical characteristics

Purchase costs are important, as some patients will have to purchase their own compressors. The cost of mains only operated devices ranged from £65 to £140, with the two multivolt options costing over £100. The annual energy consumption for 1,460 nebulizations, each of 15 min, showed a wide variation, with four units (Nos. 8, 9, 11 and 13) having an energy consumption of less than 20 $kW \cdot h^{-1}$. Moreover, there will be additional costs of replacement filters and nebulizer kits which are dependent on how the patient uses them, as well as the costs of an annual service to comply with national regulations. Weight and physical dimensions did not greatly differ. Sound level ranged from 50 dB (No. 6) up to 68 dB (No. 8). These values are in the range of a "quiet radio" (40 dB) up to "busy street traffic" (70 dB). Where sound level is important to the patient, the quieter combinations should be considered.

Different nebulizer/compressor combinations

The importance of matching the nebulizer and compressor to achieve the optimum output performance has been previously demonstrated by STEVENTON and WILSON [1]. However, from our experience the importance of this appears to have failed to reach many users in hospitals, family practice and in the community. This study has confirmed that the correct matching of nebulizer and compressor is important to achieve the optimal performance of the system. Manufacturers must, therefore, ensure that they use an appropriate combination of nebulizer and compressor, whilst the users and the purchasers of equipment must have a greater awareness of the need to correctly match the nebulizer to the compressor. We would, therefore, advise that both the compressors and the nebulizers have clearly stated recommendations to obtain optimal performance, and that suppliers provide this information to purchasers and to users of their systems.

In conclusion, the nebulizer/compressor combinations assessed in this study, show considerable variation in overall performance. The choice of a nebulizer/compressor combination should, until further work is carried out, be based on the current recommendations for flow rate at the nebulizer and particle size. From the data in this study, only nine combinations (Nos. 1A, 1B, 1C, 5, 7, 8, 9, 12 and 13) satisfy both criteria of an MMAD of less than 5 µm and a flow rate at the nebulizer of 6–8

$L \cdot min^{-1}$. As regards the NAC listed systems, only five of these combinations (Nos. 5, 7, 8, 12 and 13) are included, whilst other combinations are included which do not apparently satisfy both these criteria.

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