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A drying chamber for use with small volume jet nebulizers

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Introduction

Jet nebulizers are used to deliver a variety of drugs to the lower respiratory tract. The majority of droplets generated during the initial atomization process are too large to penetrate into the lower airways and hence baffles within nebulizers are used to generate droplets that fall within the 'respirable range' of 1–5 μm (1). In certain situations such as the 'alveolar targeting' of drugs such as pentamidine (2), it is desirable to generate droplets <3 μm in size. The use of such aerosols may also be useful in the treatment of patients with a variety of chronic obstructive airways diseases. It is known that for patients with cystic fibrosis and other such conditions, deposition of aerosols becomes increasingly more central as the disease progresses (1,3). There is evidence to suggest that finer droplets (<3 μm) may penetrate more effectively to the lung peripheries in these patients.

The standard method of generating fine aerosols, using jet nebulizers, has been to increase the effectiveness of the baffles within the system. However, the use of more effective baffles within the nebulizer itself substantially increases the time taken for a dose to be nebulized, while the use of an external baffle placed between the nebulizer and patient reduces the total dose of drug delivered. A new approach was sought in order to generate fine aerosols while maintaining the relatively high rates of drug delivery characteristic of conventional jet nebulizers.

An auxiliary chamber (volume 1 l) was designed (Fig. 1) to be used with any conventional jet nebulizer. Adjacent to the nebulizer inlet is a one-way entrainment valve and an inlet for an auxiliary 'drying' air supply. As with the nebulizers driving gas flow (DGF), the 'drying' flow could be varied as required. A series of experiments were performed in order to assess the effect on particle size of independently altering the DGF and 'drying' flow.

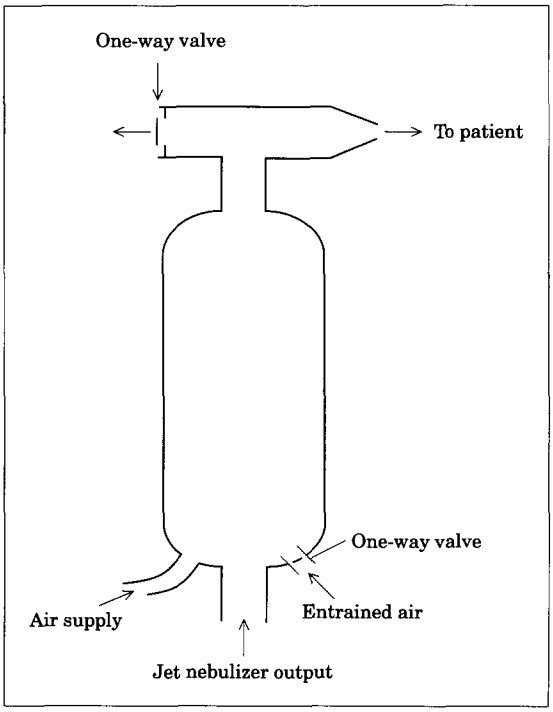

Fig. 1 Auxiliary 'drying' chamber for use with conventional jet nebulizer.

Method and Results

A Malvern 2600 particle sizer utilizing the Fraunhofer diffraction model was used to measure particle size. Two drugs in solution, gentamicin (80 mg 2 ml^{-1}) and pentamidine, and one drug suspension, budesonide (250 mg ml^{-1}) were used. The DGF and drying flow were supplied by compressed air cylinders with appropriately calibrated flow

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Table 1 Mass median diameters of aerosols generated by a Cirrus nebulizer with auxiliary 'drying' chamber when independently varying the driving gas and 'drying' gas flows. Percentages of droplet mass contained within droplets <1·22 and <4·97 μm are given for gentamicin

Driving gas flow	Drying gas flow	Gentamicin			Pentamidine	Budesonide
		MMD	% droplet mass <1·22	% droplet mass <4·97	MMD	MMD
6	0	5·4	11·4	36·6	5·3	5·4
6	6	2·2	24·8	97·5		
6	8	1·8	32·5	98·4	1·9	1·8
8	0	4·4	17·4	56·3	4·4	4·5
8	6	3·9	15·7	61·6		
8	8	1·4	42·3	95·3	1·2	1·8
8	10	1·3	45·1	96·8	1·1	1·5
10	0	2·6	21·9	75·9	2·5	2·5
10	8	2·1	31·9	84·6		
10	12	1·2	49·5	95·3	1·1	1·86

MMD, mass median diameter.

meters (BOC Medishield). A single Cirrus nebulizer (Intersurgical) was used for all the experiments. Three experiments were performed under each set of conditions.

Results obtained when nebulizing these drugs using varying DGF's and 'drying' flows are presented in Table 1. The mass median diameter (MMD) is the value such that one-half of the droplet mass is contained in larger droplets and one-half in smaller droplets. With no drying flow, the MMD increases as the DGF increases.

For each DGF, the MMD of the aerosol leaving the device is substantially reduced when the drying flow is sufficient to cause evaporation of water from the droplets. For all DGFs, MMDs of less than 1·5 μm can be achieved, the drying flow required being dependent upon the DGF.

Discussion

These results suggest that a simple drying chamber can be used with a variety of drug solutions and suspensions to significantly reduce the size of drug containing droplets being delivered to patients. Such a system is likely to significantly enhance deposition of drug in the lung peripheries, particularly in patients with airways obstruction, and reduce deposition in the upper and central conducting airways. Hence it may be of value in a variety of situations including drug delivery in patients with cystic fibrosis and the administration of drugs, such as pentamidine, which have unpleasant side-effects if deposited centrally.

The principle of 'drying' an aerosol is not novel but this is the first description we are aware of in which the principle has been applied to small volume jet nebulizers. The small particle aerosol generator (SPAG) is used for delivering ribavirin to infants with bronchiolitis (4), and it is believed that drying of the aerosol promotes delivery of the drug to the peripheral airways of small infants. However, this system is cumbersome and is designed for nebulizing large volumes of solutions over prolonged periods. The auxiliary chamber described here can be used with any conventional jet nebulizer using standard volumes of solution, and achieves greater rates of drug delivery than are possible with the SPAG.

The 'dried' particles generated by this system will be subjected to hygroscopic growth when they enter the respiratory tract but it has been estimated that hygroscopic growth is not significant until beyond the sixth generation of airways when mouth breathing (5). Hence mouth breathing will enhance peripheral penetration when inhaling hygroscopic aerosols. Theoretical calculations and experimental work suggests that for significantly hygroscopic droplets, the minimum likelihood of deposition in the airway is approximately 0·1 μm rather than 0·5 μm and that maximal alveolar deposition occurs in the range 0·5–1·5 μm (6). This range is very similar to droplet sizes that can be generated with this system.

A chamber such as this would act as a 'holding' chamber and hence would not only generate aerosols with a low MMD but would enhance drug delivery in adults by increasing the volume of aerosol that is available to be inhaled (7,8).

It should be noted that the results from Table 1 suggest that the drying flow through the chamber must be increased as the DGF increases in order to maintain a similar MMD. This presumably reflects the increased mass of droplets and water vapour passing through the chamber as the DGF increases. Acknowledging the limitations of laser diffraction for particle sizing suspensions, these results suggest that droplets containing budesonide can also be effectively dried. Indeed, it is likely that at least some of the budesonide exists as a dry powder.

Using two air supplies within the hospital setting would not be difficult. Such a system, using two standard compressors, for home use may be no more expensive than the more powerful compressors currently available, and improved drug delivery may well more than off-set the initial outlay for such a system.

In conclusion, we believe that the use of a simple drying chamber such as the one described here would be of value in situations in which it is desirable to deliver drugs as an aerosol with a low MMD, whilst still maintaining a high rate of drug delivery.

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