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Drug Delivery

Discussion guide

Advances in nebulizer technology with focus on ease of use with commonly prescribed aerosol medications

Benefits of using nebulizers for pulmonary disease management

The correct use of pressurized metered dose inhalers (pMDIs) and dry powder inhalers (DPIs) is difficult. Those who suffer from chronic obstructive pulmonary disease (COPD) are often elderly and may have reduced muscular strength, poor hand-breath coordination, reduced peak inspiratory flow and a prolonged duration of exhalation compared with younger groups of respiratory patients. Older patients are also more likely to suffer from arthritis, the after effects of stroke, cognitive disorders and neuromuscular disease.[1,2]

Nebulizers are designed to deliver drugs with normal tidal breathing, so they can be used by patients who lack the hand-breath coordination required for the use of a pMDI or a soft-mist inhaler in a single breath and who are unable to achieve the high inspiratory flows required for the correct use of DPIs.

The advanced technology of mesh nebulizers offers increased portability, quiet and efficient nebulization, and less drug left behind in the nebulizer compared to jet nebulizers.[3] Mesh nebulizers can also provide benefits to patients who have difficulty using pMDIs and DPIs due to factors such as poor coordination and impaired dexterity.[2] Table 1 presents the performance attributes of different aerosol drug delivery devices.

With vibrating mesh technology, the medication can be aerosolized rapidly, quietly and with little energy.[3] The time required to nebulize a complete dose of medication is one of the most noticeable advantages of a mesh nebulizer compared with a jet nebulizer.[3]

Table 1 Key use specifications of various aerosol delivery devices

Device	Quiet operation	Portable	Use without hand-breath coordination	Inhale with normal tidal breathing	Use with a mask
Dry powder inhaler	✔	✔	✔	✖	✖
Metered dose inhaler	✔	✔	✖	✖	✖
Compressor jet nebulizer	✖	✖	✔	✔	✔
Vibrating mesh nebulizer	✔	✔	✔	✔	✔

The InnoSpire Go offers a number of advantages during use compared with jet nebulizers and, for some patient groups, compared with pMDI and DPI inhalers.

Mesh nebulizer brands are not the same

It is important that the clinician and the user have confidence in the brand of nebulizer and the nebulizer selected for use has the right combination of performance attributes to provide an optimal treatment. Philips has over 30 years' experience developing and manufacturing nebulizers to deliver inhaled medication to patients. This experience was used in the design and development of the InnoSpire Go mesh nebulizer. The InnoSpire Go is designed to improve the user aerosol therapy experience compared with other nebulizers.

The InnoSpire Go uses Aerogen's clinically proven Vibronic vibrating mesh technology to deliver an aerosol with a particle size that targets the medication for delivery into the lungs.[4,5]

The InnoSpire Go is a portable mesh nebulizer designed to deliver aerosol treatments in approximately 4 minutes.*

*Using 2.5ml salbutamol.[6]

Overcoming the limitations of traditional jet nebulizers

Short treatment times are desirable to minimize the burden of aerosol therapy on the patient. It can be difficult to identify the end of treatment when using a jet nebulizer,[7] and treatments can last 10 to 15 minutes.[8,9] After rapidly delivering the dose, the InnoSpire Go provides an audible beep before the device automatically switches off. The technology found in InnoSpire Go shortens treatment time and eliminates the guess work regarding when the treatment ends.

Table 2 presents the treatment characteristics of the InnoSpire Go compared with common jet nebulizers.

Table 2 Treatment characteristics of InnoSpire Go compared with common jet nebulizers[10]

	InnoSpire Go	Jet nebulizer
Typical treatment time < 5 min	✔	✖
Automatic end of treatment	✔	✖
Low residual drug at end of treatment	✔	✖
Consistent treatment times	✔	✖

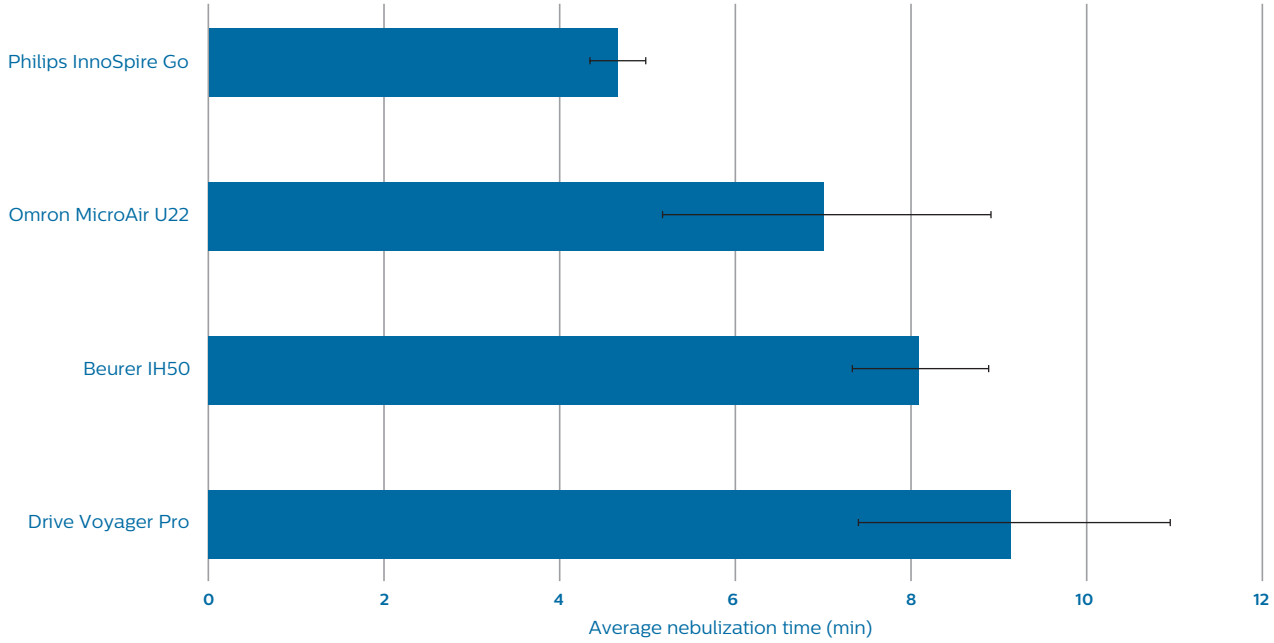
Quick treatment with little waste of medication

Shorter nebulization times may positively impact adherence to medication[11] and better adherence has been linked to better clinical outcomes.[12]

Nebulization time will be affected by the drug being nebulized and the fill volume used.

The rapid nebulization time from the InnoSpire Go has also been shown to be faster than a selection of other mesh nebulizer brands as shown in figure 1.

Figure 1 Comparison of nebulization time for delivery of 2.5 mL salbutamol sulphate (albuterol), error bars denote the standard deviation about the mean[13]



In this in vitro study performed by Slator et al., the InnoSpire Go nebulized the salbutamol in the fastest time with the smallest variation in treatment time across the four devices tested.

Designed for ease of use

Many inhaler devices are not easy to use. Incorrect use is common and is associated with poor disease control.[14, 15] Patient education and training can improve technique and use, but must be repeated frequently in order to maintain correct technique.[16]

Ease of use has been shown to be a key characteristic of aerosol drug delivery devices from the perspective of patients and one of the most important attributes identified by healthcare providers.[17] Therefore, devices that are easy to use and require minimal educational intervention would benefit all those involved in patient care.

The InnoSpire Go is designed to offer improved ease of use compared with existing mesh nebulizers. Ease of use for the InnoSpire Go was assessed during the early design stages. A commercially equivalent prototype InnoSpire Go was evaluated by a panel of participants aged 5 to 73 years, and assessed along with three other commercially available mesh nebulizers.

They were provided with a one-page quick guide for the InnoSpire Go prototype nebulizer and instructions for use leaflets for the other devices (they were not explicitly asked to use any of the instructional material). The participants were not given training in individual nebulizer use. After completing the session, participants were asked to rate the nebulizers on four attributes. InnoSpire Go received the highest ratings of the evaluated nebulizers in all four attributes, which are listed in Table 3.

Figure 2 The final InnoSpire Go design with simple two-part construction.

Table 3 Participant perception of the InnoSpire Go mesh nebulizer compared with three other commercially available mesh nebulizers[18]

Patient perception of	Areas of evaluation where the InnoSpire Go achieved the highest score compared to other mesh nebulizers
Ease of use	✔
Treatment burden	✔
Comfort of holding	✔
Appearance	✔

Other user comments identified during the handling studies allowed Philips to improve the design throughout the development process. Consequently, the final design was the result of the combination of years of experience in consumer product design paired with feedback from patients.

Capable of nebulizing commonly used medications

So that the drugs are delivered where they are needed most, it is important that the aerosol produced by the mesh nebulizer is the best size, being small enough to minimize being deposited in the mouth and upper airways. A droplet size of less than 5 micrometers (µm) is generally acknowledged to be the best size to deposit in the small airways.[19] The fine droplet fraction describes the percentage of the aerosol droplets smaller than 5 µm. The InnoSpire Go achieves the suitable particle size across a variety of medications (Table 4).

Table 4 Droplet characteristics from the InnoSpire Go, when delivering commonly used respiratory medications[20,21]

Medication	Average droplet size <5 µm	Average respirable fine droplet fraction <5 µm%
Albuterol sulfate	✔	63
Ipratropium bromide	✔	63
Dornase Alfa	✔	55
Tobramycin	✔	67
0.9% sodium chloride	✔	56
7% sodium chloride	✔	62
Sodium cromoglycate	✔	58
Budesonide	✔	52

Consistent Treatment

The droplet size of the aerosol inhaled into the lungs can affect where in the lungs the droplet is deposited,[22] and the dose delivered can affect the pharmacological and clinical effects of the drug on the patient.[23]

Zhou et al. found that different inspiratory flow rates through jet nebulizers can result in different aerosol droplet size distributions.[24] The aerosol output from jet nebulizers could be affected by the peak inspiratory flow of the user.

The aerosol droplet size from the InnoSpire Go has been shown to be relatively unaffected at constant flow rates between 15 to 30 L/min (Table 5).

Table 5 Mean (standard deviation) of Mass Median Aerodynamic Diameter (MMAD) for aerosol of 2 drugs nebulized by InnoSpire Go (n=9)[25]

	Salbutamol sulphate	Ipratropium bromide
Particle Size (MMAD) at 30 L/min (µm)	3.90 (0.37)	3.87 (0.34)
Particle Size (MMAD) at 15 L/min (µm)	3.99 (0.26)	3.93 (0.27)
Relative difference (%)	2.3	1.5

Additionally, tests using simulated breathing patterns with peak inspiratory flows between approximately 11 and 65 L/min have demonstrated a low dose variability of the InnoSpire Go compared with two types of jet nebulizer (Table 6).

Table 6 Variability of delivered dose across simulated breathing patterns representing patients with high and low peak inhalation flows[26]

Device	Dose variability
InnoSpire Go	0.12 mg
Open vent jet nebulizer	0.42 mg
Breath enhanced jet nebulizer	0.55 mg

There was less dose variability from the InnoSpire Go across the range of peak inhalation flows, which would result in more consistent treatment regardless of the effect of disease severity on the peak inhalation flow of the user.

Summary

The InnoSpire Go rapidly delivers commonly used respiratory medications to the lungs.

The InnoSpire Go is easy to use compared with other mesh nebulizers.

The InnoSpire Go offers a number of advantages during use compared with jet nebulizers and, for some patient groups, compared with pMDI and DPI inhalers.

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